



Evaluation of Routine Serum Biochemical Parameters and Inflammatory Markers in Apparently Healthy Stone Quarry Workers of Chamarajanagar.

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KEYWORDS

Biochemical parameters, Inflammatory response, Interleukin-6, Serum ferritin, Stone quarrying.

ABSTRACT:

Introduction: Stone dusts which arise during quarrying of dimension stones consists of silicate particles, iron, lead and other trace metal ores. Chronic exposure to silica dust is associated with pulmonary fibrosis, Interstitial lung disease and lung cancer. In the initial stages, silica dust inhalation is known to elicit an inflammatory response.

Aims and objectives: The objective of the study is to estimate and compare the levels of routine Biochemical parameters, acute phase reactant and inflammatory markers in stone quarry workers with non-exposed individuals.

Methods: This is a prospective cross-sectional study. Forty apparently healthy stone quarry workers and forty age matched non-dust exposed healthy individuals underwent biochemical investigations which included blood glucose, ferritin, Interleukin-6, renal and liver function tests. Their vital and anthropometric parameters were recorded.

Statistical analysis: Descriptive statistics data is expressed as mean and standard deviation (SD). Pearson's correlation is used to find relationship between variables and Chi-square test to find association between the attributes.

Results: The mean \pm SD of pulse rate ($p=0.0009$), systolic blood pressure ($p=0.0094$), blood urea ($p=0.0018$) and serum creatinine ($p=0.0018$) was significantly higher in stone quarry workers group compared to the controls. A positive correlation existed between years of exposure to dust with serum ferritin levels among stone quarry workers who have been working in quarries between six and ten years ($r=0.4853$; $p=0.0484$).

Conclusions: The present study recommends periodic screening of stone quarry workers, as inflammatory response sets-in way before the surfacing of the clinical manifestations in these individuals.

1. Introduction

India is a major reserve of dimension stones in the world. The dimension stones principally include granite, limestone, marble, sand stone and slate. These dimension stones are extracted from natural rock beds on the Earth's exposed surface by quarrying. The dimension stone quarrying industry in India employs over one million

people comprised primarily of semi-skilled people from the rural areas. Karnataka harbours around 20% of the stone resources of India [1]. Stone quarrying is one of the common occupations of people residing in Chamarajanagar, the southernmost district of Karnataka. Quarries on one hand provide employment to the lower socio-economic strata of the population, however on the



other hand this occupation is accompanied with unwarranted health hazards.

Stone quarrying activities involve drilling, blasting and extracting which generates lot of dust. Stone dusts thus formed typically consists of silicate particles, iron, lead and other trace metal ores. Silica comprises over 47 % of the quarry dust [2]. Workers exposed to stone quarry dust have high probability of developing lung disease called silicosis. Silica is less than 10 microns in size and enter the lungs directly through respiration which over a period of time considerably reduces the lung capacity [3] The initial stages of silica exposure is asymptomatic as these particles are odourless and non-irritant. Chronic exposure to silica dust is associated with pulmonary fibrosis, Interstitial lung disease, lung cancer and various other pulmonary diseases. Further, exposure to silica dust and occurrence of silicosis predisposes to Pulmonary Tuberculosis [4].

Chronic silicosis is often a radiological finding. In the initial stages silica dust inhalation is known to elicit an inflammatory response. There are many studies which reports abnormal lung function tests [5], haematological indices [6], raised ESR and serum total protein [7], C-reactive protein [2] in stone quarry workers, However, the quest for a potential specific early biomarker for silicosis continues.

Alexander Hedbrant et al have conducted a study in 2023 on forty labourers working at Swedish iron foundries in whom they have estimated inflammatory markers pre and post work-shifts. They have reported that respirable quartz exposure correlated with several NLRP3 inflammasome-related markers, including plasma levels of interleukin-1 β (IL-1 β) and interleukin-18 (IL-18) [8]. Joe-Jesus Blanco Perez et al in their prospective observational study published in the year 2021 in Spain have revealed that inflammatory markers like interleukin-8(IL-8), alpha-1antitrypsin (AAT), C-reactive protein (CRP), ferritin and Lactate dehydrogenase (LDH) were elevated in stone quarry workers exposed to silica. They also have found that IL-8, LDH and AAT levels were associated with progression of silicosis and IL-6, IL-8, LDH, AAT, ferritin, and CRP with vital status [9]. El Shafy WS et al in their research project at Sokhna, published in the year 2018 studying the impact of dust exposure in stone quarry workers on ventilatory functions and serum

Tumor necrosis factor- α have observed mild to moderate impairment in ventilatory functions and elevated levels of serum TNF- α levels in dust exposed quarry workers compared to non-exposed people. A positive correlation between duration of exposure and levels of inflammatory markers has also been reported [10] Fathed S Al- Otaibi et al have studied the impact of stone quarrying on functions of different organs among stone quarry workers of Riyadh and Libyan Jirds in 2018 by estimating serum transaminases, creatinine, Malondialdehyde and glutathione. A significant elevation in serum transaminases, creatinine, Malondialdehyde levels were noted and a reduction in serum glutathione was observed [11]. A one-year follow-up study by Jong Seong Lee et al on coal-mine workers in the year 2010 have observed that the inflammatory markers serum Interleukin-8 (IL-8) and Tumour necrosis factor- α (TNF- α) were significantly elevated in workers with coal workers' pneumoconiosis (CWP). They also found that higher levels of IL-8 were associated with the presence of CWP and elevated serum TNF- α levels were associated with progression of CWP [12].

There is dearth of research pertaining to status of routine biochemical test values, acute phase reactant levels and inflammatory biomarkers in stone quarry workers in this region of South India. Our study is an attempt to provide biochemical perspective to aid early diagnosis of silicosis in stone quarry workers.

2. Objectives

The aim of the study is to identify one or more deranged routine or Inflammatory parameter among stone quarry workers which can be utilized as a cost effective and early biomarker in its effect

The primary objective

- To estimate routine Biochemical parameters, acute phase reactants and inflammatory markers in stone quarry workers of Chamarajanagar
- To measure the levels of the same biochemical indices in healthy non-exposed individuals.

The secondary objective is to compare the levels of Biochemical parameters, acute phase reactants and inflammatory markers between stone quarry workers and healthy non-exposed individuals of Chamarajanagar



3. Methods

This is a prospective cross-sectional study. The study was conducted in Clinical Biochemistry Laboratory of the Institute in the month of December 2023. The Institutional Ethics committee approval was taken before the commencement of the study. An informed written consent was obtained from each one who participated in the study.

Sample size calculation: The sample size of number stone workers who constitute Cases (group I) and healthy volunteer comprising Controls (group II) was determined using the equation mentioned below.

$$\text{Sample size, } n = N/1 + Ne^2$$

Where N = Population size

e = margin of error (For 95 % Confidence interval, Margin error = 0.05)

Considering the labour population in each quarry to be five in number in total nine quarries in and around Chamarajanagar

$$N = 9 \times 5 = 45$$

$$\text{Sample size } n = 45/1 + 45 \times 0.05 \times 0.05$$

$$n = 40$$

Source of data: The study subjects involve two groups of people

First group: Cases

Inclusion criteria:

1. Forty workers above 18 years of age who are apparently healthy and are working in stone quarries operating in and around Chamarajanagar.

Exclusion criteria

1. Workers with history of medical or surgical illness
2. Pregnant and lactating women
3. Workers on any kind of medications
4. Workers with acute illness/ active infection/allergies

A detailed history about working hours, years spent working in quarries, personal habits like tobacco use, smoking and alcoholism, dietary habits of the workers was recorded.

Second group: Controls:

Forty age and sex matched healthy volunteers who have no history of exposure to stone quarry dust.

The participants in both the groups underwent general physical examination, where their vitals like pulse, respiratory rate and blood pressure were recorded. They were examined clinically to rule out conditions like pallor, icterus, koilonychia, oedema etc. The anthropometric indices which included height and weight measurement of the study subjects was also recorded and body mass index (BMI) was calculated. With this data we ensured that clinically apparently healthy individuals were inducted into this research project.

5 ml fasting venous blood sample was drawn under all aseptic precautions from the participants of both groups and the following assay was performed:

1. Fasting Blood Glucose: by Hexokinase method
2. Blood urea: By Urease method
3. Creatinine: By Jaffe's Kinetic method
4. Liver function tests:

| | |
|---|----------------|
| a) Total bilirubin | } Diazo method |
| b) Direct Bilirubin | |
| c) Aspartate transaminase (AST): -UV kinetic without PLP method | |
| d) Alkaline phosphatase (ALP): PNP AMP kinetic method | |
| e) Total protein- Biuret method | |
| f) Albumin-BCG method | |

All these above tests were processed on Erba XL-640 fully automated chemistry analyser

5. Serum Ferritin -Chemiluminescence immunoassay
 6. Serum Interleukin-6 (IL-6) - Chemiluminescence immunoassay
- The above two tests were analysed on Maglumi-800 fully automated Chemiluminescence based analyser.

After performing the tests, the values were tabulated and compared between Cases and control using a suitable statistical tool.



Statistical analysis:

Data collected is analysed using descriptive and inferential statistics on software Microsoft excel and SPSS v23. The demographic data is expressed as frequency and percentages. Descriptive statistics data is expressed as mean and standard deviation. Pearson's correlation is used to find relationship between variables. To find association between the attributes Chi-square test is used. Student 't' test is utilized to find significant difference between the groups of the study. All the statistical analysis will be carried out at 5 % level of significance and p value of < 0.05 will be considered significant.

4. Results

The stone quarry workers who were part of the study were all men and therefore healthy non-exposed individuals in the control group selected were also men. Table 1 is a compilation of Mean and standard deviation (SD) values of vitals, anthropometric and biochemical parameters measured in cases and controls. There is a significant difference in pulse rate, systolic blood pressure, blood urea, serum creatinine and Uric acid (UA) levels between Cases and Controls.

5. Discussion

The international organisations such as the World Health Organisation (WHO) and International Labour organisation (ILO) have taken initiatives expressing their commitment towards achieving health, safety and resilience at work places for the general public across the world [13,14]. In India, the Ministry of Labour and employment in their preamble have mentioned on being obligated to review National policy on safety, health and environment at work places in the country [15]. At the outset preventive measures minimizes the risk of occupational hazard, however periodic health check-up of workers facilitates detection of health hazard at an early stage when cure is possible. In the present study we have done clinical and biochemical examination of stone quarry worker who are asymptomatic.

The comparison of vital parameters between cases and controls in the study has revealed that the mean pulse rate and systolic blood pressure is significantly higher in stone quarry workers as compared to non-exposed healthy individuals as shown in Table 1. Lohe N and Gosh S have reported similar findings in their study

which was conducted on stone quarry workers of Nagaland, India. The workers had significantly high Blood pressure, pulse rate, body mass index, oxygen saturation and forced vital capacity (FVC) of the lungs than the normal healthy individuals [4]. In the current study there was no significant difference in the anthropometric measurements between cases and controls.

Among the biochemical parameters that were compared which is depicted in Table 1, a statistically significant difference was observed with comparatively higher levels of blood urea and serum creatinine in cases as compared to the controls. This is in accordance with the research conducted by Bama R et al who also reported significantly high blood urea, serum creatinine and uric acid levels in their study group who were the stone quarry workers as compared to controls [16]. In the present study there is statistically significant difference in uric acid levels between cases and controls, though here the uric acid levels are higher in controls than in cases. Uric acid is a potent anti-oxidant present in the circulation [17], the levels being higher in healthy controls is probably a sign of a good anti-oxidant reserve in non-exposed individuals when compared to dust exposed workers having low levels.

There was no significant difference in any of the liver function test parameters between the cases and the controls unlike studies by Richard EE et al and Ilahi I et al whose findings reveal significantly higher levels of some LFT parameters like Total bilirubin (TB), conjugated bilirubin (CB), alanine transaminase (ALT), alkaline phosphatase (ALP) and aspartate transaminase (AST) among stone dust exposed individuals [18, 19].

The chief biochemical parameters in the current study are serum ferritin and Interleukin-6 which are inflammatory markers. When these two analytes were estimated and evaluated in both the groups of the project, we noticed that though there was no significant difference in their levels between the two groups, however, the mean \pm SD of ferritin as well as IL-6 was found to be higher among the cases than the controls (Table 1). Among the cases 12.5 % that is, five workers had high serum ferritin levels and 32.5 % (13 workers) had abnormal IL-6 levels which is quiet alarming. Similar findings of elevated serum ferritin in individuals with silicosis was reported by Aloe C et al [20]. Ferritin



is an acute phase reactant [21] and the abnormal ferritin in five stone quarry workers only suggest the inflammatory response cascade that has probably set-in in these individuals. Elevated IL-6 in silica exposed workers was also brought to light by Blanco-Pérez et al in their research project [9]. Interleukin-6 is a multifactorial cytokine secreted by lymphocytes, monocytes, pulmonary fibroblasts and macrophages. Release of IL-6 levels will exert effects on other inflammatory factors and immune cells which are associated with silica-induced pulmonary fibrosis [22]. IL-6 has the potential to generate dust-mediated oxidative stress in the lungs [23].

When we segregated the forty quarry workers based on duration of years spent working in the quarry into four sub-groups, we noticed that thirteen (32.5%) and seventeen (42.5%) men fell in 1-5 years and 6-10 years exposure interval sub-group respectively. There were seven (17.5%) who fell in sub-group 11 to 15 years' and three (7.5%) have been working in quarry for more than 16 years. Twenty-three percent (03/13) men among less than five years exposure sub-group had elevated ferritin. Forty-one percent (07/17) stone quarry workers in sub-group 6 to 10 years had high IL-6 levels. This data is presented in Table 2.

When a correlation analysis between years of exposure with serum ferritin and IL-6 levels was done for the whole group of forty stone quarry workers in case-group we did not find any statistically significant association which can be noticed in Table 3.

Pearson's correlation analysis data which is compiled in Table 4, revealed a positively significant correlation between exposure to dust with serum ferritin in stone quarry workers group who have worked in quarries between six to ten years. This is because we have highest number of workers under this sub-group compared to other three sub-groups. The small sample size in the remaining three sub-groups is probably the reason behind not finding a significant year of exposure to serum level correlation for ferritin. Unlike ferritin, IL-6 has a narrow reference interval. To obtain a statistically significant correlation for a parameter like IL-6 we require a larger population which is a key shortcoming of this project.

Chronic exposure to dust causes deposition of silica particles in the lung alveoli which are engulfed by the

macrophages. This induces an inflammatory response which causes release of inflammatory cytokines such as IL-6, IL-1 β and TNF- α . The release of inflammatory compounds stimulates proliferation of fibroblasts ensuing in collagen synthesis eventually causing lung fibrosis [24].

Limitations of the study: Small sample size

Conclusion:

The awareness about health hazard risk to an individual working in stone quarry industry is explicit. The workers seek medical assistance only when they present with certain symptoms and signs of a disease. The present study has successfully proven the importance that these workers should undergo periodic health check-up and routine screening, as apparently healthy doesn't mean "absence of disease". The research project has shown a statistically significant increase in vital and renal parameters values in dust exposed workers as against non-exposed healthy adults. The study could not however endorse any of the assessed biochemical analyte as a potential early predictor of inflammatory events that originates in these workers. At the end we recommend researchers to take forward the study to a larger stone quarry worker population with a follow-up.

Conflict of interest: None

Note: This study was selected for ICMR STS-2023 program.

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