

### **338. Surveillance of sensitization and adverse health effects assessment by low molecular weight organic acid anhydrides exposure in the Site Area Kotri, Jamshoro, Pakistan.**

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#### **Abstract**

The major aim of this present study was to explore the exposure-response effects of harmful chemicals organic acid anhydrides (OAAs) frequently used in polymer and different industries including chemical (n=50), paint(n=70), plastic(n=30), dye(n=50) and Pharmaceuticals (n=50) compared with control (n=150) of same age groups (20-60yrs). The Serum total protein, serum Albumin and Hemoglobin levels were evaluated clinically. All of the diseases linked with protein abnormalities to check liver and kidney functions. The demographic study of all of worker groups (n=250) was done by questionnaire, medical history and addictions habits were also obtained. The comparison of serum total protein showed no significant difference ( $p>0.05$ ), but the serum albumin of plastic industry ( $p>0.01$ ) and dye industry ( $p>0.05$ ) workers found below the normal range. The Hemoglobin was significantly decreased ( $p>0.05$ ) among all of worker groups than control (non-exposed) may revealed the prevalence of Anemia. This suggests that changes in serum protein after exposure to anhydrides may play the key role behind the pathogenesis of allergy and hypersensitivity among workers, SITE Area, Kotri.

**Keywords:** harmful; serum albumin; anemia; allergy; anhydrides.

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## 1. INTRODUCTION

It has been reported that differently extensively used organic acid anhydrides (OAAs) possess varying sensitize potential due to structure, physical and chemical properties. These anhydrides have potential to induce various health issues like Rhinitis, Asthma, allergy, conjunctivitis and cancer among exposed workers [1-2].

Basically the occupational exposure may have two types of toxic effects such as respiratory and allergy symptoms [3]. The occupational asthma was reported by Maleic anhydride (M.A) use in Insecticides and Immunoglobulin antibody IgE level in serum confirmed the sensitization in exposed workers [4]. These low molecular weight compounds may bind with protein after exposure to form adducts complex by nucleophilic addition or substitution reaction. They have an ability to become associated with Biomacromolecules like Serum albumin (SA) or Hemoglobin (Hb) in blood [5].

Various anhydrides were reported for causing sensitizing symptoms as Maleic anhydride(MA), Phthalic anhydride(PA), trimellitic anhydride(TMA) and methylhexahydrophthalic anhydride (MHHPA) [6-9]. The occupational Rhinitis and asthma were frequent among workers after 8 yrs exposure time span. The smoking increased the risk effects and eyes, nose, pharynx symptoms [10]. Ocular airways and respiratory symptoms were found in powder paints contain OAAs. The asthma was frequent among large population of workers [11].

As the protein has got supreme status in metabolism and present in all body major functions. The allergenic anhydrides adducts with two major blood plasma proteins like hemoglobin(Hb) and serum albumin(SA) in workers have already been reported[12]. There is not so much work reported on metabolic protein role and this present study was especially done to find protein differences among different exposed workers (n=250) groups clinically compared with control.

## 2. MATERIALS & METHODS

### 2.1 Methodology

The intravenous blood (10 ml) samples each for industrial workers groups like Chemical industry (n=50), Paint industry (n=70), Plastic industry(n=30), Dye industry(n=50),

Pharmaceuticals industry(n=50) and healthy subjects(n=150) were collected and serum was separated accordingly. This serum was collected and stored at 40 °C prior to analysis by kit method for total protein and albumin(kit method is given in protocol Table 3.8). The hemoglobin test was done on whole blood by Dark bin's solution.(Microlab). The standards and reagents were of Merck company (Germany) analysed.

## **2.2 Medical examination survey of workers**

All workers studied in this research study were divided into different groups. They were employed at chemical industry, paint industry section, dye industry (Textiles), Plastic industry and Pharmaceuticals. The OAAs (organic acid anhydrides) were handled in ventilated hood or closed system, but some manual operations were performed at elevated temperatures (approx. 60-80°C). All workers had been exposed for many years prior to this research study. The workers were invited to participate in an extensive study on exposures to anhydrides and their health effects. The plasma samples were obtained by these groups of workers and serum was also obtained from plasma.

## **2.3 Collection of blood samples**

All human blood samples for plasma were collected into 10ml sampling tubes containing anticoagulant (EDTA or sodium heparin). The blood was allowed to cool after sampling at room temperature and centrifuged at 6500 r.p.m for about 10min.

The blood plasma was separated into layers. The clear serum layer was transferred into another clean micro centrifuge tubes and saved. The whole blood was re-suspended in test tube centrifuged again at 13000 r.p.m for 5min. we had two samples such as serum sample, another red blood cell sample were stored at -20°C.

## **2.4 Ethics**

All the samples were obtained by workers will to give blood plasma and medical history by questionnaires supplemented with interviews by research scholar and local physician.

## 2.5 Medical examination

Extensive occupational and medical histories including addictions like smoking, Betel nut chalia, Main puri habits were obtained with the help of self administered questionnaires (given below in Figure 1) by a physician. Even the information about current work tasks (Painting, Chemical industry, Plastic industry, Dyes) at the present workplace, symptoms such as from the eyes (Scratching, Itching, Burning, Runny); from the nose (Blocked, Runny, Itchy attacks of sneezing) ; from lower airways (Cough, Asthma, Chest infection) ; and from skin(allergy, eczema) were collected.

<b>BIODATA (MEDICAL HISTORY)</b>			
No of worker:-----			
Time:-----			
Date:-----			
Name:-----			
Address:-----			
Profession:-----Age:-----Sex: Male/Female			
Work task : Painting/ Chemical industry/Plastic industry/Dyes/Insecticides/ Pesticides/Pharmaceuticals.			
<b>Exposure time:</b>	Years:	Months:	Days:
<b>Symptoms ( if any):</b>			
<b>Duration of disease ( if any):</b>	Yes/No		
<b>Drug history :</b>	Yes/No		
<b>Smoking/ Beetle nut/ main puri/Paan</b>	Yes/No		
<b>Eyes: Scratching/Itching /Burning/Runny</b>	Yes/No		
<b>Nose: Blocked/Runny/Itchy attacks of sneezing</b>	Yes/No		
<b>Cough/Asthma/Chest infection</b>	Yes/No		
<b>Skin allergy/ Eczema</b>	Yes/No		
<b>Fever</b>	Yes/No		

Fig. 1. Questionnaire of the studied subjects(workers)

### 3.RESULTS & DISSCUSSIONS

The clinical data for all of industries including Chemical, Paint, Plastic, Dye (Textile) and Pharmaceuticals are given in table 1 below.

**Table.1:Demographic results of normal subjects (non-exposed to anhydrides) and exposed workers groups with OAAs**

Group	M(n)	Age, Mean $\pm$ SEM
Control	150	42 $\pm$ 1.9
Chemical industry	50	55 $\pm$ 2.1
Paint industry	70	34 $\pm$ 1.7
Plastic industry	30	49.8 $\pm$ 3.4
Dye industry	50	50 $\pm$ 2.3
Pharmaceuticals	50	38 $\pm$ 1.5

**(Note: Mean  $\pm$ SEM stands for standard error Mean values.)**

The total protein, Serum Albumin and Hemoglobin (Hb) were determined on Microlab 300 by Kit Method System, Merck. The total protein levels may slightly increase in case of hypertension, liver cirrhosis and Diabetes. Serum albumin levels are related with liver disorders as it is produced in liver as major protein. The abnormal Serum albumin levels are found in kidney or liver diseases and even malnutrition. The prevalence of anemia with low Hb<12 mg/dl (found in men) reflects the hemoglobin role in the early stages of kidney diseases and other factors.

The total protein of all of workers groups including Chemical, Paint, Plastic, Dye (Textile) and Pharmaceuticals are found in normal range along with control group and significant.

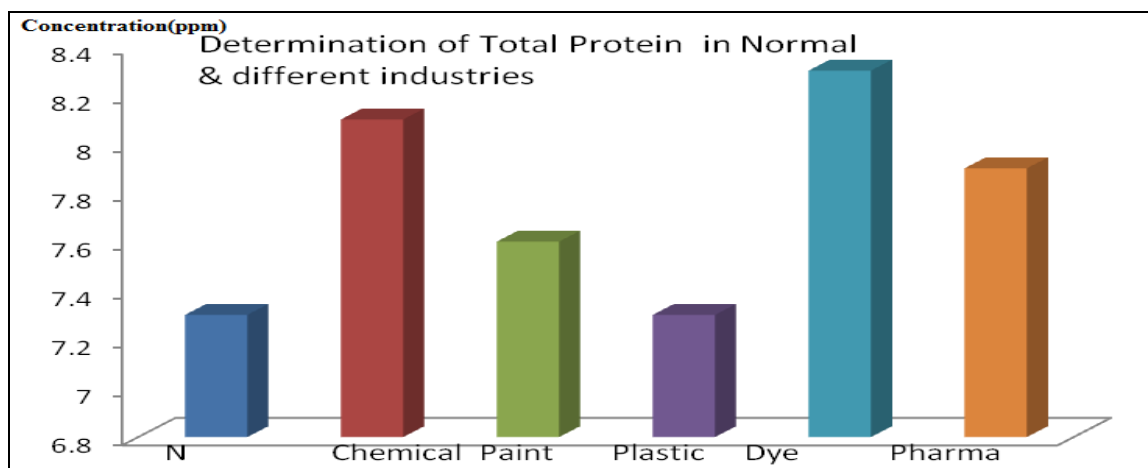


Fig. 2. Total protein levels (ppm) in normal & different industries, Site Area, Kotri.

Table . 2 Levels of serum total proteins in normal & different industries, Site Area, Kotri

Group	M(n)	(T.P), Mean $\pm$ SEM
Control	150	7.3 $\pm$ 0.08
Chemical industry	50	8.1 $\pm$ 0.10*
Paint industry	70	7.6 $\pm$ 0.2*
Plastic industry	30	7.3 $\pm$ 0.1**
Dye industry	50	8.3 $\pm$ 0.1*
Pharmaceuticals	50	7.9 $\pm$ 0.18***

\* P<0.05, \*\* P< 0.01, \*\*\* P< 0.001

The Serum Albumin of plastic and dye industry are below normal range, while chemical and pharmaceuticals are in normal range.

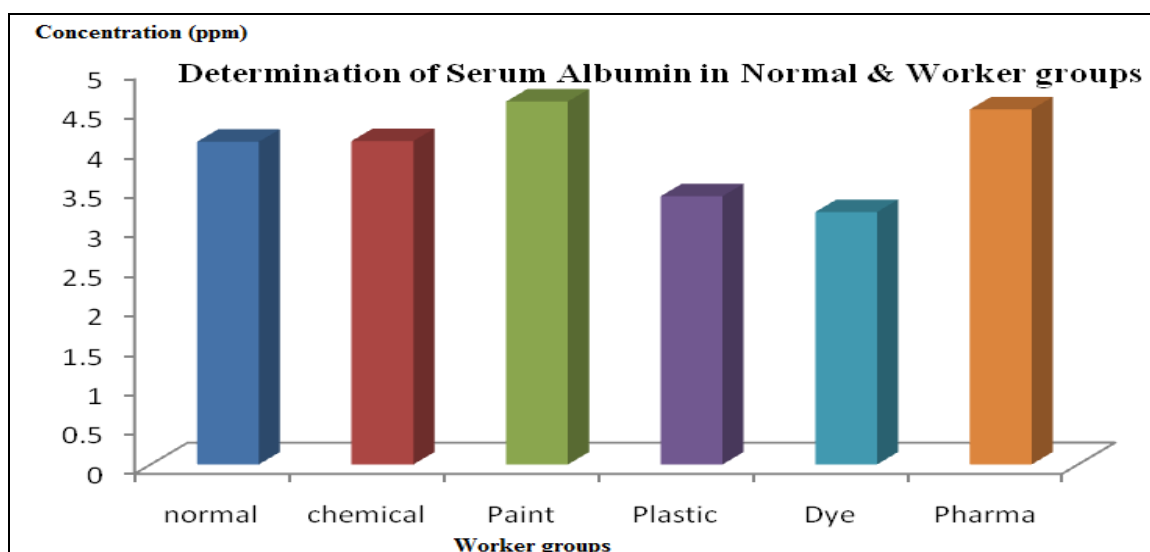


Fig. 3 Serum Albumin levels in normal & different industries, Site Area, Kotri.

Table 3. Levels of serum albumin in normal & different industries, Site Area, Kotri

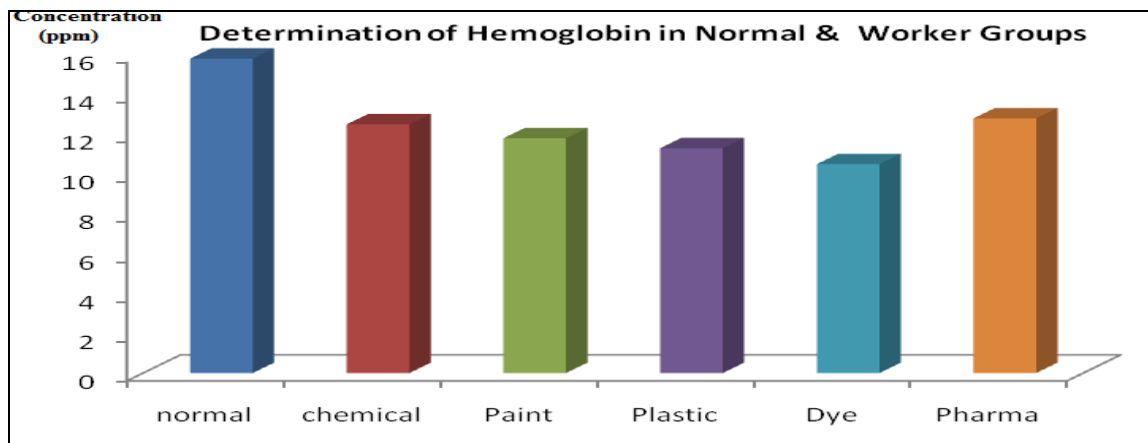
Group	M(n)	(S.A), Mean $\pm$ SEM
Control	150	4.09 $\pm$ 0.1
Chemical industry	50	4.1 $\pm$ 0.16**
Paint industry	70	4.6 $\pm$ 0.1*
Plastic industry	30	3.4 $\pm$ 0.12*
Dye industry	50	3.2 $\pm$ 0.2***
Pharmaceuticals	50	4.5 $\pm$ 0.1*

\*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$

(Note: Unit Mean  $\pm$  SEM stands for standard error mean.)

The Hemoglobin of all industry worker groups are low values shows prevalence of anemia. Most of the blood samples did not meet the normal limits less than 14g/dl (as shown in graph no.1). Almost 75% of samples in workers were found to be affected by anemia by showing low hemoglobin (Hb) values and adverse health impacts after exposure. Anemia with lower hemoglobin (Hb) levels also associated with early stages of developing diseases like chronic Kidney disease (CKD), diabetes, cardiovascular and even heart failure in worst conditions(

Mohanram et al., 2004).



**Fig.4 Hemoglobin levels (ppm) in normal & different industries, Site Area, Kotri**

**Table 4. Levels of Hemoglobin in normal & different industries, Site Area, Kotri**

Group	M(n)	(S.A), Mean $\pm$ SEM
Control	150	15.8 $\pm$ 1.4
Chemical industry	50	12.5 $\pm$ 1.1*
Paint industry	70	11.8 $\pm$ 0.9*
Plastic industry	30	11.3 $\pm$ 0.5*
Dye industry	50	10.5 $\pm$ 1.2***
Pharmaceuticals	50	12.8 $\pm$ 1.3*

**P<0.05, \*\* P< 0.01, \*\*\* P< 0.001**

The Demographic results study showed the control (non-exposed to OAAs) and the workers (exposed to OAAs) as in figure. The data collected from all male (n=400) individuals are divided into two major groups including control (non-exposed to OAAs) and exposed workers to OAAs. The exposed workers (OAAs) are further divided into five groups comprising the chemical industry (n=50), paint industry (n=70), plastic industry (n=30), dye industry (n=50) and Pharmaceuticals (n=50). Many workers were already having allergic and asthmatic problems. The



blood plasma from control (n=150) and exposed Workers (n=250) were examined for total protein, Serum albumin and Hemoglobin.

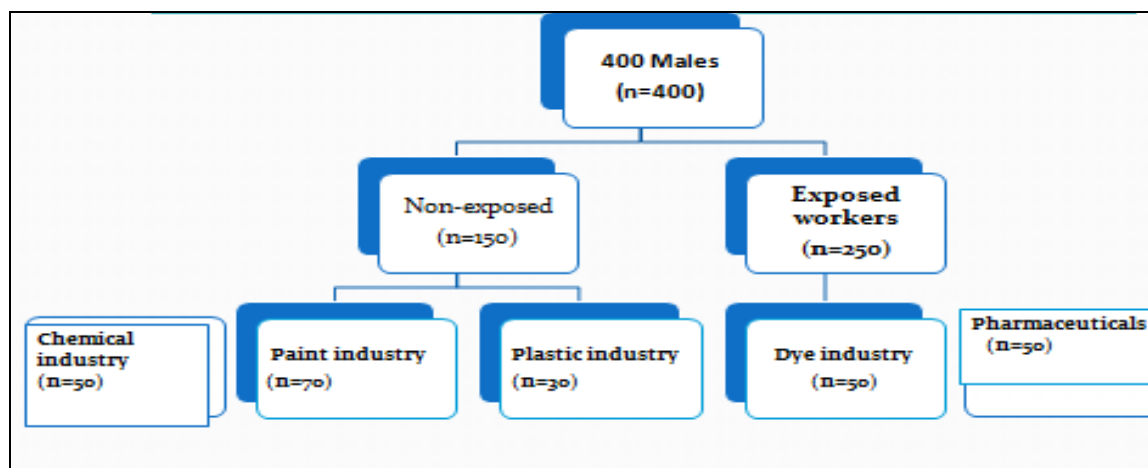


Fig 5. The number of non-exposed control and exposed (OAs) Workers for different groups of workers.

The demographic studies revealed that many workers were already having allergic and asthmatic problems. We found many workers with various allergic problems like eczema, itching, Wheezing, dry cough and asthma due to occupational activities from many years. Our studies also correlates with the previous findings also indicating the work related symptoms from eyes (burning, itching, lacrimation):airways(chest tightness, wheezing, dyspnoea) ; nose (sneezing, bleeding, runny, blocked),smoking or other addictions habits (beetle nut , Beetle leaf or Paan) may having linked for enhancing effects [14-15].Extensive medical histories from workers also showed one worker groups smoking, while other worker groups does not smoking with habits (Beetle nut, Beetle leaf and drinking liquor). The both age factor and smoking (for many years) may be the risk factors for respiratory and allergy complications in exposed workers.

## 5. CONCLUSION

This whole research study demonstrated the potential risk of frequently used industrial chemicals like cyclic anhydrides and the health status of exposed workers in SITE Area, Kotri, Sindh, Pakistan.

## 6. Acknowledgement

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## 7. REFERENCES

1. X. D. Zhang, P.D.Siegel and D.M.Lewis," Immunotoxicology of organic acid anhydrides (OAAs)" *International Immunopharmacology*.,Vol 2,2002,pp. 239-248.
2. R.D. Barker ,M.J Tongeren ,J.M.Harris, K.Gardiner, K.M.Venables and A.J.Newman Taylor," Risk factors for bronchial hyperresponsiveness in workers exposed to acid anhydrides",*European Respiratory Journal*.,Vol. 15,2000,pp.710-715.
3. K.M. Venables, " Low molecular weight chemicals, hypersensitivity, and direct toxicity: the acid anhydrides", *Br. J. Ind. Med.* ,Vol.46,1989, 222-232.
4. J.R.Ingelfinger, "Occupational Asthma" *N.Engl.*,Vol37,2014,pp.640-649.
5. M. Tornqvist, C. Fred, J. Haglund, H. Helleberg, B. Paulsson and P. Rydberg, "Protein adducts: quantitative and qualitative aspects of their formation, analysis and applications",*Journal of Chromatography B*., Vol.778,2002, pp.279-308.
6. P.F.G. Gannon, P.S. Burge, C. Hewlett and R.D. Tee," Haemolytic anaemia in a case of occupational asthma due to maleic anhydride" *Br. J. Ind. Med.*,Vol.49,1992,pp.142-143.
7. C. A. Maccia, I.L. Bernstein, E.A. Emmett and S.M. Brooks, In vitro demonstration of specific IgE in phthalic anhydride hypersensitivity",*Am Rev Respir Dis*.,Vol.113, 1976, 701-704.
8. L.C. Grammer, A. M. Tripathi and K.E. Harris, " Prevalence and onset of rhinitis and conjunctivitis in subjects with occupational asthma caused by trimellitic anhydride (TMA)" *J. Occup. Environ. Med.*,VOL.44,2002,pp.1179-1181.
9. P.Pfaffli., M. Hameila and R. Riala," Exposure to methylhexahydrophthalic anhydride (MHHPA) in two workplaces of the electric industry", , *J. Occup. Environ. Med.*, Vol.6,2004,pp. 295-299.
10. J.Nielsen ,H. Welinder , I.Bensryd ,L. Rylander ,S. Skerfving , "Ocular and airway symptoms related to organic acid anhydride exposure- a prospective study" *Allergy*, Vol. 61,2006, pp. 743-49.
11. S.M.Tarlo and C. Lemiere," Occupational Asthma review",*N.Eng.J.Med.*,Vol.370,2014,pp.640-649.
12. S.Qureshi,S.A.Memon,A.J.Laghari and A.B.Ghanghro," Metabolic total protein investigation in local industry workers exposed to acid anhydrides", *SURJ*.,Vol. 41,2009,pp. 63-66.
13. A.Mohanram, Z.Zhang, S.Shahinfer,W.Kene, B.Brenner, R.Toto," Anemia and end stage of renal diseases in patients with Type 2 Diabetes and nephropathy", *Kidney Int.*,Vol. 66,2004,pp. 1131-1138.

14. G.Johannesson,S.Rosqvist,C.H.Lindh,H.Welinder and B.Jonsson,"Serum albumins are the major site for in vivo formation of hapten-carrier protein adducts in the plasma from humans and guineapigs exposed to type-1 allergy inducing organic acid anhydrides", Clin.Exp.Allergy,Vol.31,pp.1021-1030.
15. S.Qureshi,S.A.Memon,A.B.Ghanghro,M.A.Mughal and S.Khan," Electrophoretic analysis of Serum Proteins in Workers Exposed to OAAs", International Journal of Multidisciplinary Sciences and engineering,Vol.4,2013,pp.65-68.