Effects of Bauxite and Alumina Exposure on Incidence of Cancer - Meta-analysis

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ABSTRACT

Bauxite is an ore from which Aluminium is produced. Malaysia, once the leading producer of bauxite has reduced production as mining activity has caused community outrage. Due to concerns about health concerns, rising pollution and environmental hazards, the government has revoked the licenses of bauxite miners. We therefore did a meta-analysis to assess the relationship between exposure to Bauxite and Alumina with incidence of various types of cancers. Bauxite mines and alumina refineries. Individuals of all ages exposed to Bauxite and Alumina. Exposure to bauxite and alumina. Incidence due to overall cancers and specific types of cancers.

Exposure to bauxite and alumina did not cause variations in incidence of overall cancer and specific types of cancer such as cancer of lip, cancer of the oral cavity and pharynx, cancer of digestive organs and others. We conclude that there is no evidence that bauxite or alumina exposure cause increase incidence of cancer but due to the small number of studies included in this review, we recommend more cohort studies to be done in future.

KEY WORDS

Bauxite alumina exposure, Cancer incidence

INTRODUCTION

Malaysia was once the world's top procedure of Bauxite which could bring revenue for the country and increase employment. French chemist Henri Sainte-Claire Deville named the mineral "bauxite".[1] Bauxite ore is named after the town Les Baux in France where it was first found. Most bauxite reserves are found in the area within the tropics of Cancer and Capricorn with key areas in West Africa, South America South east Asia and Australia.[2]

In Malaysia, annual output of bauxite ore increased from a little over 200,000 tons in 2013, to nearly 20 million tons in 2016 making the nation one of the world's top producers of bauxite in 2016.[3]

There has been community outrage on the hazards of bauxite mining and aluminium processing. There are postulations that even though chronic diseases are not apparent, they may appear later due to the slow pathogenesis.

Bauxite and alumina mining throughout the world have resulted in community outrage due to their concerns on environmental and health issues. Bauxite, an ore, is the world's main source of Aluminium. Donoghue et al. found that the most important risks of bauxite mining and aluminium processing were related to noise, ergonomics, trauma, and caustic soda splashes of the skin/eyes.[4] Other risks of note were related to fatigue, heat, solar ultraviolet and for some operations tropical diseases. Donoghue at al noted that exposure to Bauxite dust was not related to decrements in lung function and association with cancer.[5]

Basic Science

i) Description of the exposure

Bauxite is a group of aluminium oxides, with the term denoting the economically most important mixture of these minerals.5 The importance of Bauxite is that it is regarded as the primary ore of the metal aluminium. Bauxite is further classified according to its commercial application, such as refractory, abrasive, cement, chemical and metallurgical. Of all bauxite mined, approximately 85% is converted to alumina (Al_2O_3) for the production of aluminum metal, a

further 10% is utilized for nonmetal uses as various forms of specialty alumina, and the remaining 5% is used for non-metallurgical bauxite applications.[6]

ii) How the exposure might relate to mortality

Both bauxite and alumina dusts are considered as insoluble low-toxicity dusts. Though there have been no consistent associations with respiratory symptoms or lung functions with either dusts, high exposure to alumina has been associated with scanty, small irregular opacities in the lungs.[7-9] Benke et al. further noted workers in bauxite and alumina refineries to be possibly associated with radiographic abnormalities on lungs.[10] In addition, workers exposed to dusty jobs, irrespective of dust type, are at risk to heart disease risk factors through inflammatory changes in blood vessels.[11,12] Quartz is approximately 3% of respirable bauxite dust, which is approximately 30% of inhalable bauxite, so some silica exposure occurs which in the form of respirable, crystalline silica has been noted as risk factor for non-malignant respiratory disease and lung carcinogen.[13-16]

iii) Importance of this review

However as a result of concerns on health concerns and other issues such as rising pollution, and environmental hazards, Malaysia has banned mining activities on bauxite and alumina.[3]

Internal comparisons among individuals and especially workers exposed to bauxite and alumina have shown some evidence of associations with malignancy (especially pleural mesothelioma), circulatory, cardiovascular and cerebrovascular disease which was not seen in external comparisons.[17]

Although bauxite and alumina mining have been around for many decades, there is lack of literature with regards to the hazards of bauxite mining. Abdullah et al. postulate that even though chronic physical illnesses are not apparent now due to its slow pathogenesis, diseases may appear later on if not properly addressed and controlled.[18]

To our knowledge, there has been no review anywhere in the literature on the effects of exposure towards bauxite and alumina on the mortality as a result of malignancy, circulatory, cardiovascular and cerebrovascular disease among individuals such as workers in the mining industry and population residing nearby these industries.

The objective of this study is to assess the relationship between exposure to bauxite and alumina with incidences of various types of diseases.

METHODOLOGY

This review included cohort studies of individuals of all ages who were exposed to bauxite and alumina. The outcomes studied were incidence of overall cancer and other specific types of cancers.

We obtained relevant studies from Pubmed, Google Scholar, Science Direct and Cochrane Library using the words Bauxite, Alumina, Aluminium Oxide, cancer, specific types of cancer. The last search was done on 10th October 2017. We obtained full texts through the Ministry of Health Virtual Library and the Library of Melaka Manipal Medical College, Malaysia.

The two review authors (TT and ALA) assessed the eligibility of the studies independently and subsequently scrutinized and verified the studies to be entered. We settled and solved disagreements through discussion. Full texts of all the articles were obtained.

The review authors perused and independently selected the studies. We settled disputes by going through the studies together with further discussion.

We assessed exposed and unexposed from same population (selection bias), assessment of exposure (assessment exposure bias), absence of outcome at start (outcome bias), presence of prognostic variables / confounders (presence confounder bias), adjustment for prognostic variables / confounders (adjust confounder bias), assessment of outcome (assess outcome bias), adequacy of follow-up (follow-up bias), similar co-intervention between groups (co-intervention bias). The risks of bias were assessed as low risk, unclear risk and high risk.

We carried out meta-analysis via the use of Review Manager software (RevMan 2014) for the trials that were eligible. We utilized fixed-effect meta-analysis model for trials that were sufficiently similar with no significant heterogeneity. We made use of risk ratio or mean differences as summary measures where applicable.

We used the Chi^2 test for heterogeneity with significance level $p < 0.1$ and assessed the degree of heterogeneity by means of the I^2 statistic. I^2 value of 30% or more was regarded as having moderate heterogeneity.

We made extensive searches in an attempt to reduce and minimise publication and reporting biases. Selective outcome reporting was assessed within studies as part of risk of bias assessment. We had initially aimed to utilise funnel plot analysis to assess for publication bias; however as there were insufficient studies with similar outcome measures, we did not perform these funnel plot analysis.

We had planned to carry out a sensitivity analysis to explore the effects of the risk of bias of the studies and thereafter by excluding trials with a high risk of bias for this domain. However, we did not proceed to perform the analysis as there were insufficient trials with similar outcome measure in this review.

RESULTS

We obtained and searched seven records related to the topic, of which all records were identified through

database searching MEDLINE, PubMed, Google Scholar and the Cochrane Library (fig. 1). There was no other record identified from other sources.

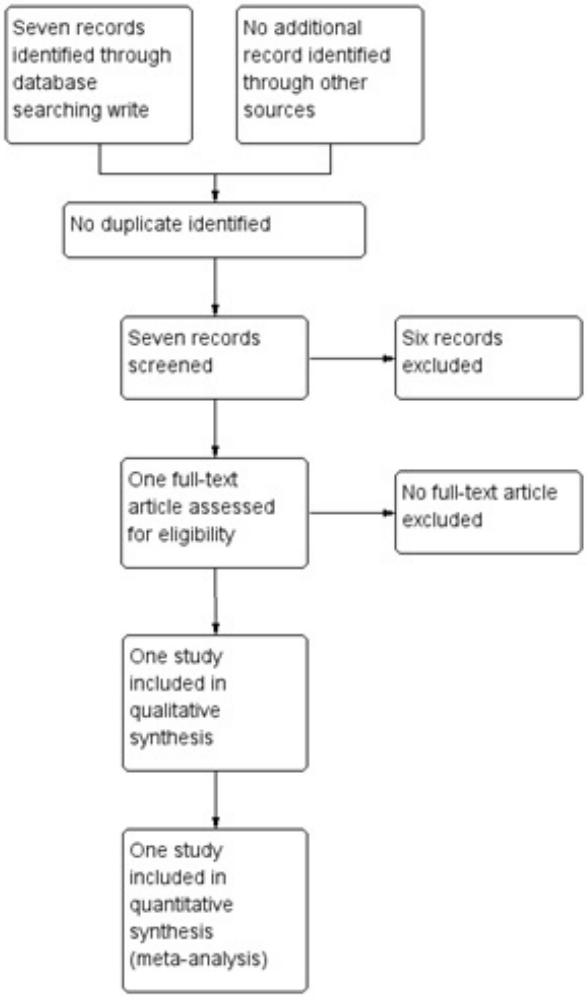

Figure 1. Flow Chart-Selection of Studies for Inclusion

We further acquired the full-text publication for all seven studies. We proceeded to remove six records from this list that did not fully fulfill the inclusion criteria, leaving us a total of one study.

We included one cohort study that met our inclusion criteria. This study consisted of 6485 employees who further comprised of 5828 men and 657 women (Table 1). Fritschi 200 817 followed up former and current employees of a large aluminium company as long as they had been employed for at least 90 days at any of the bauxite mines or alumina refineries on or after January 1983.

We excluded 6 studies which did not fully fulfil the inclusion criteria -Donoghue 2014, Benke 1998, Friesen 2009, Fritschi 2001, O'Connor 2013, Kusim 2016.[4,10,13,19,20,21]

We analysed outcomes which included incidence of overall cancer, and other specific types of cancer such as cancer of lip, cancer of the oral cavity and pharynx, cancer of digestive organs, cancer of respiratory and intrathoracic cancer, melanoma, mesothelioma, cancer of male genital organs, urinary tract cancer, cancer of brain and central nervous system, cancer of thyroid, endocrine cancer, leukaemia and lymphomas.

Table 1. Characteristics of included study – Fritschi 2008.[17]

Methods	Cohort Study
Participants	Employees comprising 5828 exposed to bauxite and alumina working in mines/refineries and a further 1437 as control (ever office), mean age 29.0 years.
Exposure	Bauxite and alumina
Outcomes	Incidence of various types of cancer such as cancer of lip, cancer of the oral cavity and pharynx, cancer of digestive organs, cancer of respiratory and intrathoracic cancer, melanoma, mesothelioma, cancer of male genital organs, urinary tract cancer, cancer of brain and central nervous system, cancer of thyroid, endocrine cancer, leukaemia and lymphomas.

In Fritschi 2008, participants comprised of employees taken from the bauxite mines or alumina refineries. Selection bias was categorized as low risk as these employees had the same point of origin with regards to the population group.[17]

Fritschi 2008, did not provide details of how exposure information was obtained.[17] Though the study mentioned that employees without job history information were excluded from the analysis, the study mentioned that work histories of employees between 1996 and 2002 were not made available. The study is thus categorized as having an unclear risk of bias with regards to assessment of exposure.

In Fritschi 2008, the outcome measured included incidence of cases of cancer which were recorded after initiation of study. We therefore classified the study as having low risk bias in this domain.[17]

In Fritschi 2008, sex and 5-year age group were identified for standardization purposes as these were regarded as plausible prognostic variables.[17] However there was no mention of other potential prognostic variables such as smoking status and exposure to other carcinogens, for instance asbestos and hence we categorised the study as having unclear risk of bias

Fritschi 2008, reported the use of standardisation performed for certain plausible prognostic variables only such as sex, 5-year age group and calendar year.[17] However, we assessed adjustment was performed for only some of the plausible prognostic variables and hence classified the study as having uncertain risk of bias.

In Fritschi 2008, the outcomes comprised of incidence which were as they acquire the illness. We thus categorised the study as having low risk of bias with regards to assessment of outcome.[17]

The study Fritschi 2008, had reported complete follow-up data where participants are made up of employees taken from the bauxite mines or alumina refineries. We had therefore classified the study as having low risk bias in this domain.[17]

Table 2. Risk of bias – Fritschi 2008.[17]

Bias	Authors' judgement	Support for judgement
Exposed and unexposed from same population (selection bias)	Low risk	Employees taken from the bauxite mines or alumina refineries on or after 1st January 1983
Assessment of exposure (assessment exposure bias)	Unclear risk	Not mentioned
Absence of outcome at start (outcome bias)	Low risk	Outcome included incidence which were recorded after initiation of study
Presence of prognostic variables / confounders (presence confounder bias)	Unclear risk	Not mentioned other potential confounders – smoking status, exposure to other carcinogens such as asbestos, etc.
Adjustment for prognostic variables / confounders (adjust confounder bias)	Unclear risk	Standardization performed for certain variables only - sex, 5-year age group and calendar year. Not done however on other potential confounders – smoking status, etc.
Assessment of outcome (assess outcome bias)	Low risk	Outcomes comprised of incidence which were recorded according to specific causes of deaths.
Adequacy of Follow-up (Follow-up bias)	Low risk	Employees taken from the bauxite mines or alumina refineries were followed up for the duration of study
Similar co-intervention between groups (Co-intervention bias)	Unclear risk	Not mentioned

We categorised the study Fritschi 2008, as having unclear risk of presence of co-intervention bias as there was no mention of documentation of relevant co-interventions in the exposed and non-exposed.[17]

Exposure towards bauxite and alumina had no differences with regards to incidence of overall cancer when compared to control (RR 0.87, 95% CI 0.68 to 1.10; Table 3 and Figure 2).

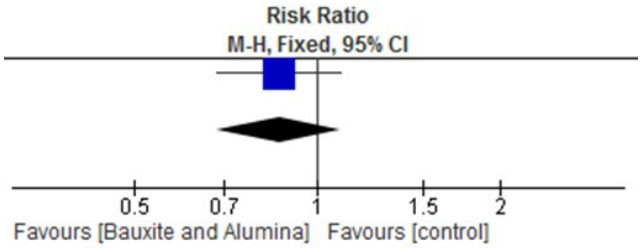

Figure 2. Forest Plot-Incidence of Overall Cancer Among Those Exposed to Bauxite and Alumina.

We observed no association between exposure towards bauxite and alumina with incidence of any of the specific cancers measured – cancer of lip, oral cavity, pharynx (RR 1.05, 95% CI 0.35 to 3.11; Table 3); cancer of digestive organs (RR 0.75, 95% CI 0.46 to 1.24); respiratory, intrathoracic cancer (RR 0.58, 95% CI 0.31 to 1.08); melanoma (RR 1.17, 95% CI 0.63 to 2.18); mesothelioma (RR 0.74, 95% CI 0.20 to 2.73); cancer of male genital organ (RR 0.63, 95% CI 0.38 to 1.05); urinary tract cancer (RR 0.92, 95% CI 0.31 to 2.78); cancer of brain / CNS (RR 3.70, 95% CI 0.21 to 64.75); cancer of thyroid / endocrine (RR 0.37, 95% CI 0.10 to 1.31); leukaemia, lymphoma (RR 0.62, 95% CI 0.24 to 1.59).

DISCUSSION

We noted that exposure towards bauxite and alumina did not have an effect on incidence due to or incidence of overall cancers (cancel due to) overall cancers. In addition, exposure towards these metals did not have an effect on incidence of specific cancers such as cancer of lip, cancer of the oral cavity and pharynx, cancer of digestive organs, and cancer of respiratory and intrathoracic. Incidence of other forms of cancer such as melanoma, mesothelioma, male genital organs, urinary tract, brain and central nervous system, thyroid, endocrine, leukaemia and lymphomas were all noted not to have any changes in risk ratios towards bauxite and alumina.

Although the number of trials is small, we conclude that the exposure to bauxite and alumina was not associated with differences in incidence due to overall cancer and specific types of cancer.

We observed that the trial evidence was generally of good quality with a low risk of bias. We identified seven records but excluded six as they did not fulfill our inclusion criteria. The employees had the same point of origin and all completed the study. Incidences of cancer were the outcomes measured.

The trial did not show differences in incidence of cancer due to exposure to Alumina and Bauxite. Potential biases such as the job history, prognostic variables and co-interventions were not mentioned during the review process.

CONCLUSION

There is no evidence to show that exposure to bauxite and alumina will cause an increased incidence of overall cancer and specific types of cancer.

Initial results show that there is no association between bauxite and alumina exposure with increase in incidence of overall cancer, and other specific types of cancer such as cancer of lip, cancer of the oral cavity and pharynx, cancer of digestive organs, cancer of respiratory and intrathoracic cancer, melanoma, mesothelioma, cancer of male genital organs, urinary tract cancer, cancer of brain and central nervous system, cancer of thyroid, endocrine cancer, leukaemia and lymphomas.

Table 3. Incidence of overall cancer, other selected forms of cancer among those exposed to Bauxite and Alumina versus non-exposure

Cancer category	Bauxite and Alumina		Control			Risk Ratio	Test for Overall Effect, Z	P value
	Events	Total	Events	Total	Weight	M-H,Fixed, 95% CI		
Overall Cancer								
Fritschi 2008	295	5828	84	1437	100%	0.87 [0.68, 1.10]		
Total (95% CI)		5828		1437	100%	0.87 [0.68, 1.10]	1.20	0.23
Lip, oral cavity, pharynx								
Fritschi 2008	17	5828	4	1437	100%	1.05 [0.35, 3.11]		
Total (95% CI)		5828		1437	100%	1.05 [0.35, 3.11]	0.08	0.93
Digestive organs								
Fritschi 2008	61	5828	20	1437	100%	0.75 [0.46, 1.24]		
Total (95% CI)		5828		1437	100%	0.75 [0.46, 1.24]	1.11	0.27
Respiratory, intrathoracic								
Fritschi 2008	33	5828	14	1437	100%	0.58 [0.31, 1.08]		
Total (95% CI)		5828		1437	100%	0.58 [0.31, 1.08]	1.71	0.09
Melanoma								
Fritschi 2008	57	5828	12	1437	100%	1.17 [0.63, 2.18]		
Total (95% CI)		5828		1437	100%	1.17 [0.63, 2.18]	0.50	0.62
Mesothelioma								
Fritschi 2008	9	5828	3	1437	100%	0.74 [0.20, 2.73]		
Total (95% CI)		5828		1437	100%	0.74 [0.20, 2.73]	0.45	0.65
Male genital organ								
Fritschi 2008	51	5828	20	1437	100%	0.63 [0.38, 1.05]		
Total (95% CI)		5828		1437	100%	0.63 [0.38, 1.05]	1.77	0.08
Urinary tract								
Fritschi 2008	15	5828	4	1437	100%	0.92 [0.31, 2.78]		
Total (95% CI)		5828		1437	100%	0.92 [0.31, 2.78]	0.14	0.89
Brain, CNS								
Fritschi 2008	7	5828	0	1437	100%	3.70 [0.21, 64.75]		
Total (95% CI)		5828		1437	100%	3.70 [0.21, 64.75]	0.90	0.37
Thyroid, endocrine								
Fritschi 2008	6	5828	4	1437	100%	0.37 [0.10, 1.31]		
Total (95% CI)		5828		1437	100%	0.37 [0.10, 1.31]	1.54	0.12
Lymphoid, haematopoietic (leukaemia, lymphoma)								
Fritschi 2008	15	5828	6	1437	100%	0.62 [0.24, 1.59]		
Total (95% CI)		5828		1437	100%	0.62 [0.24, 1.59]	1.00	0.32

RECOMMENDATION

This is the first systematic review on incidence of cancer as a result of exposure towards alumina and bauxite.

The strengths of this review included focusing only on the most definitive of observational study designs which were cohort studies, using appropriate search engines for identification of studies and applying relevant risk of bias for the included studies.

Though extensive search was made, the literature was language restricted to English. We hope to see more individual cohort studies performed globally on alumina and bauxite which would further increase the number of included studies in future meta-analyses.

We hope this study will be a useful tool to guide policy makers and miners on information pertaining to Bauxite and Alumina mining.

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