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Research Article

ROLE OF HEAVY METALS (LEAD AND CADMIUM) IN MALIGNANT BREAST TUMORS

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ABSTRACT
Heavy metals as environmental pollutants have been recognized to have a role in the induction of malignant human growths. Recently, certain heavy metals have shown a close association with breast cancers. The objective of this study was to assess the concentration of lead and cadmium in malignant breast tumors and the normal breast tissue of the same individual. Lead and Cadmium concentration was determined in the breast tissue samples of 30 malignant breast tumor patients. Two samples of breast tissue from each patient, i.e. diseased tissue and normal tissue (from the same breast of the same patient) were taken during the lumpectomy or mastectomy procedure, for analysis by atomic absorption spectrophotometer. The present study showed a highly significant increase in Lead (11.8 ± 2.6) ($P < 0.001$) and Cadmium (6.5 ± 1.9) ($P < 0.001$) concentrations in malignant breast tumor tissues as compared to their corresponding normal tissues (Lead 4.4 ± 2.7 and Cadmium 1.9 ± 1.1). We concluded that Lead and Cadmium have a significant role in the causation of malignant breast tumors and can be a potent diagnostic marker of the disease process.
Keywords: Lead, Cadmium, Malignant Breast Tumor, Atomic absorption spectrophotometer.

INTRODUCTION

Breast diseases are very common all over the world; especially malignant breast tumors are common in the western world. Breast cancer ranks second to all cancers in the American women and incidence of female breast cancer has risen world wide in the recent decade.[1,2] In India, breast cancer is the most common cancer among women in many regions and has overtaken cervix cancer.[3] Presently the percentage of breast cancer among the male population has risen above 2 % of all cancers.[4,5]

There are various risk factors for breast cancer which include estrogenic and reproductive factors, hereditary factor, dietary factor, environmental factors and also life style of the individual.[1,2] Heavy metals as environmental pollutants have been implicated in human carcinogenesis by various researchers.[6,7] The present study has been undertaken to estimate the role of cadmium and lead in the causation of malignant breast tumors.

MATERIAL AND METHODS

The present study was conducted in the Department of Surgery, Ajmal Khan Tibbiya College and the Departments of Pharmacology and Pathology, J.N. Medical College, A.M.U, Aligarh, India on 30 malignant breast tumors patients aged 15-65 years of age.

A detailed medical history and a thorough systemic examination with routine haemogram, urine for routine and microscopic examination, random blood sugar and X-ray chest were performed. Mastectomy/lumpectomy was done under general anesthesia/local anesthesia and about 1 g of diseased breast tissue was dissected and dissolved in 4 ml of acid (3 ml Nitric acid + 1 ml Perchloric acid) in a compressed vial, after trimming of fat and stored until analyzed. The normal tissue (taken from the same breast of the same patient 2 cm away from the tumor) and diseased tissue were analyzed for heavy metals - lead and cadmium by atomic absorption spectrophotometer (4139 ECIL). The statistical analysis was done by applying student't' test.

RESULTS

The age of the patients ranged from 15 to 65 years, with a mean age of (43.8 ± 12.7 years). There were 28 females (93.3 %) and 02 males (6.7 %) in our study, with female: male ratio of 14:1 (Table 1). Tissue lead levels in malignant breast tumors ranged from 8.04 to 16.6 µg/g (mean11.8 ± 2.6) (Table 2). Maximum number of patients of malignant breast tumor group, 14 (46.7 %) had tissue lead levels in the range of 8.0 - 12.0 µg/g. There was a highly significant difference in lead levels between normal tissue and diseased tissue group ($t = 10.8$, $p < 0.001$). Tissue cadmium levels in malignant breast tumor group are ranged from 2.8 to 9.4 µg/g (mean 6.5 ± 1.9) (Table 3). Also a significant difference in tissue cadmium level was noted between normal tissue and diseased tissue of malignant breast tumor group ($t = 12.2$, $p < 0.001$).

DISCUSSION

Lead and cadmium are known carcinogens and we have tried to establish the fact that heavy metals have a close association in breast cancer development. Previous studies have also stated that a close association exists between heavy metals like lead and cadmium and breast cancer development.[6,7] Researches even suggests that exposure to cadmium had significant risk of developing ovarian as well as renal cancer.[2] Singh *et al* have concluded presence of high concentration of heavy metals in gall bladder cancer patients, indicating a possible role of heavy metals in gall bladder carcinogenesis.[8]

Table 1: Distribution of Malignant breast tumor cases and controls according to Sex

SEX	Malignant Breast Tumor		Controls	
	Number	Percentage	Number	Percentage
Male	2	6.7	10	50.0
Female	28	93.3	10	50.0
Total	30	100	20	100

Table 2: Tissue Lead levels in µg/g, in malignant breast tumor and controls

Tissue lead level (in µg/g)	Malignant breast tumor			
	Tumor Tissue		Normal Tissue	
	No. of cases	Percentage	No. of cases	Percentage
0-4	–	–	16	53.3
4.01-8	4	13.3	8	26.7
8.01-12	14	46.7	6	20
12.01-16	10	33.3	--	--
16.01-above	2	6.7	--	--
Total	30	100	30	100
Mean ± S.D	11.80 ± 2.6		4.42 ± 2.8	

Table 3: Tissue Cadmium levels in µg/g, in malignant breast tumor and controls

Tissue Cadmium level (in µg/g)	Malignant breast tumor			
	Tumor Tissue		Normal Tissue	
	No. of cases	Percentage	No. of cases	Percentage
0 - 2	--	--	20	66.7
2.01 - 4	03	10.0	07	23.3
4.01 - 6	13	43.3	03	10.0
6.01 - 8	05	16.7	--	--
8.01 - above	09	30.0	--	--
Total	30	100	30	100
Mean ± S.D	6.48 ± 1.89		1.58 ± 1.10	

In our study, out of thirty malignant breast tumor patients, twenty-eight (93.3 %) were females and two were males (6.7 %), a finding concordant with the study of Hussain *et al*,[5] who reported 4 % incidence of breast cancer in males. Another study done in England and Wales showed that the incidence of female breast cancer has risen in the recent decade with increase in male breast cancer.[9] The present study revealed that the mean tissue cadmium levels (6.5 ± 1.9) in malignant breast tumor group was significantly higher than in the normal tissue ($t = 14.6$, $p < 0.001$). This is in variance with the study done by Erkki *et al*[10] who reported that the mean cadmium concentration in 43 cancer patients did not differ significantly from 32 healthy controls. They accounted that the high concentrations of tissue cadmium was due to the characteristic feature of cadmium, being tightly bound to adipose tissue and poorly excreted in the milk. Ionescu *et al*[11] have found that cadmium level was significantly higher in cancer biopsies than healthy control group, in their study on 20 frozen breast cancer biopsies. Also Dora Il' yasova and Schwartz[12] has also documented that occupational exposure to cadmium was associated with increased risk of renal cancer. Abo El Atta *et al*[13] through an *in vitro* study using normal cultured mammary cells and breast cancer cells, to find out the possible mechanism for cadmium induced breast cancer, reported that cadmium chloride is cytotoxic to primary cultured cells and induced DNA damage in both mammary cultured cells and breast cancer cells, due to the mutations in their nucleotide sequence. They advocated that cadmium could be considered as a chemical carcinogen; that may act either as an initiator or promoter to mammary cancer. Mona A El-Harouny[14] in their study on 100 female patients (75 cancerous and 25 non-cancerous), established the fact that heavy metals had some role in the induction of malignant human growth, especially breast cancer. The heavy metal concentrations of cadmium showed a significant increase in urine and breast tissue in cancerous patients as compared to non-cancerous ones ($p < 0.05$), and thus helped establish a causal association between cadmium and breast cancer. Eliane Kellen *et al*[15] conducted a study to assess the relationship between exposure to cadmium and bladder cancer risk and suggested that individuals with increased exposure to cadmium had an increased risk of bladder cancer. Phillip and Hughes[16] studied the residents of Shipham Village, Somerset, England, who were exposed to high soil levels of cadmium and demonstrated a small but statistically significant risk for carcinoma of the ovary in the cadmium exposed population. Strumylaite *et al*[17] underwent a study on 57 breast cancer patients and 51 benign diseases and concluded that the average cadmium concentration in malignant tumors was significantly higher than in benign tissues, with no significant difference in healthy tissues between both groups. In the current study, the mean lead levels in malignant breast tumor group (11.8 ± 2.6), was significantly higher ($t = 10.8$, $p < 0.001$) than the normal tissue group (4.4 ± 2.7), a finding discordant with Mona El Harouny,[14] who showed that there was no significant difference in lead levels between cancerous and non-cancerous group. Edgar Drake and Sky-Peck[6] in their study on trace element distribution in normal and malignant human tissue, reported low levels of lead in lung tumors as compared to normal lung tissues with a significant difference between the two tissues. Mulay *et al*[18] also showed low level of lead in malignant tissues than normal tissues. Ellen K *et al*[19] in their study on the carcinogenic activity of lead, suggested that its role in carcinogenesis was permissive rather than causative, that is, lead may be able to increase the risk of cancer by reducing the ability of the cell to protect or repair DNA damaged by other exposures, rather than by causing alterations in DNA directly. Higher levels of cadmium, lead and mercury was also reported by Iman Al Saleh and

Shinwari[20] in brain tumor patients. Ionescu *et al*[11] demonstrated a significant increase in lead and zinc concentration of patients with breast cancer and accounted the effects to their ability to generate hydroxyl radicals leading to lipid peroxidation, DNA strand breaks and apoptosis. Palus J in 2003[21] studied to assess the genotoxic damage in somatic cells of workers in a Polish battery plant after high-level occupational exposure to lead and cadmium and concluded that lead and cadmium induce clastogenic as well as aneugenic effects in peripheral lymphocytes, indicating a potential health risk for working populations with significant exposures to these heavy metals.

CONCLUSION

A marked variation in the levels of lead and cadmium in malignant breast tumors and normal tissues with a markedly high level in malignant tumor tissues was seen in our study, asserting a risk of malignant transformation on prolonged exposure to these heavy metals.

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