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# HERIDITARY PATTERN OF CANCER

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***SUMMARY***

*Three thousand nine hundred and twelve patients with cancer in various sites reporting to the out patient department were questioned for history of cancer among blood relatives. A positive history of cancer was obtained in 154 of whom 89 were male and 65 female. Thirty nine patients gave history of cancer among siblings and five gave history of cancer among spouses related by consanguneous marriage. The other 110 gave history of cancer among second and third generation relatives. Sixty one percent maternal relatives of the female patients had cancer as compared to only 33 percent of paternal relatives. This difference was not seen among male patients where there were about 45 percent of maternal and 47 paternal relatives giving history of cancer. Further it was found that 6 of 20 patients with cancer of the breast, 7 of 22 with stomach cancer and 4 of 12 with cervix cancer had blood relatives with the same type of cancer.*

## INTRODUCTION

Familial aggregation has been reported for virtually every form of cancer in human[6]. An inherited susceptibility to cancer often becomes apparent through the occurrence of the same neoplasm among multiple blood relatives and these neoplasms tend to occur at earlier ages than usual and from multiple foci[1,4]. Identification of cancer types with familial risk will help in early disease detection and also avoidance of harmful exposure to carcinogens will delay the onset of neoplasia in familial cancers that are triggered by environmental. influences[3]. So this study aims at finding out the familial pattern of cancer among cancer patients, and to examine the occurrence of neoplasm at the same site in more than one generation (Clustering).

## MATERIALS AND METHODS

There were 3912 patients with different forms of cancer registered in the Department of Oncology, Government General Hospital between January 88 to December 91, out of whom 154, gave history of cancer among blood relatives. Patients giving history of cancer among distant relatives, in-laws, neighbours or friends were not considered for the analysis. All the records contained detailed information of the Cancer site, information of the blood relative(s) of the cancer patients treated by the department and also their exact relation to the patient traced upto the third

generation. The confirmation of cancer among cases is by (i) biopsy report sent by the referring physician and (ii) biopsy that was done at the Medical Oncology, Government General Hospital, Madras. The confirmation of cancer among family member is (i) by getting history from the patient and (ii) from the records of previous treatment in the same hospital. Information regarding cancer sites in index cases and relatives, and type of relationships to index cases was extracted from the hospital records for analysis.

Generations have been defined as follows : the third generation relatives of the Index case consists of Paternal Grand Father (PGF) and Grand Mother (PGM) and Maternal Grand Father (MGF) and Grand Mother (MGM), the second generation relative consists of Father (F), Mother (M), Paternal Uncle (PU) and Aunt (PA) and Maternal Uncle (MU) and Aunt (MA) and the first generation is the patient siblings and spouse (Consanguneous marriage).

## RESULTS

Out of the 3912 case records studied, 154 (3.9%) patients with primary malignancy gave history of cancer in one or more blood relatives. Among 154 patients with family history 89 (58%) were males and 65 (42%) were females. Of these 44 belonged to the first generation and 110 to the second and third generations. Age ranged between 18-85 years for males and 17-70 years for females. The primary site of cancer for cases with family history of malignancy is shown in Table I. History of malignancies among relatives was observed more frequently in patients presenting with cancers of pharynx, breast, cervix, colon, stomach and ovaries than in other forms of cancers. Similar pattern was seen in those with cancer caecum eventhough the numbers were very small.

**Table - I**

**Familial History In Different Sites Of Cancers**

| Site | Total No. of Patients Attending the OP | Family H/O Cancer No | % |
|---|---|---|---|
| 1. Caecum | 8 | 2 | 25 |
| 2. Pharynx | 77 | 12 | 16 |
| 3. Breast | 267 | 20 | 8 |
| 4. Cervix | 148 | 12 | 8 |
| 5. Colon | 76 | 6 | 8 |
| 6. Ovary | 157 | 11 | 7 |
| 7. M.S. Organ | 93 | 5 | 5 |
| 8. Uri. System | 78 | 4 | 5 |
| 9. Rectum | 78 | 4 | 5 |
| 10. Larynx | 95 | 4 | 4 |
| 11. Stomach | 559 | 22 | 4 |
| 12. Esophagus | 116 | 5 | 4 |
| 13. Brain | 121 | 3 | 3 |
| 14. Lymphatic | 547 | 12 | 2 |
| 15. Liver | 161 | 1 | 1 |
| 16. Lung | 385 | 3 | 1 |
| 17. Others | 948 | 28 | 4 |

Most patients with family history had more than one relative affected (Table II). Gastrointestinal system cancers accounted for 53% of cancers in males and breast and gynaecological cancers predominated among females (66%). Forty four (2%) of cancer patients with family history had only first generation relatives with cancer and 51% of them had only second generation relatives

**Table II**

**Number Of Blood Relatives With Cancer By Sex**

| Index Case | | | | | | |
|---|---|---|---|---|---|---|
| No. of relatives with cancer | Male | | Female | | Total | |
| | No. | % | No. | % | No. | % |
| 1 | 68 | 76.4 | 53 | 81.5 | 121 | 78.6 |
| 2 | 16 | 18.0 | 9 | 13.9 | 25 | 16.2 |
| 3 | 2 | 2.2 | 3 | 4.6 | 5 | 3.2 |
| 4 | 2 | 2.2 | 0 | 0.0 | 2 | 1.3 |
| 5 | 1 | 1.1 | 0 | 0.0 | 1 | 0.6 |
| TOTAL | 89 | 100 | 65 | 100 | 154 | 100 |

affected by malignancy and 8% of them had only third generation relatives suffering from Cancer. Even (7%) of the Cancer patients with positive family history had first and second generations relatives with cancer, 6 (4%) had second and third generation relatives with cancer and one patient had first and third generation relatives with cancer (Figure 1).

Regarding the familial pattern of cancer (Table III). i.e. cancer from the second and third generation relatives, male cancer patients with positive family history were

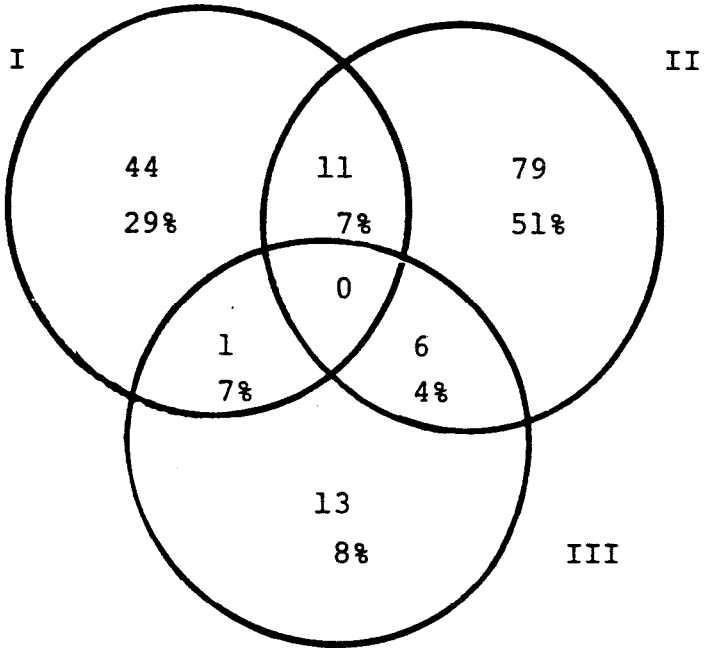


***Fig. : Diagram dipicting the three generation with History of Cancer.***

**Table III**

**History of Familial Cancer Among Paternal And Maternal Relatives of Second and Third Generation Relatives**

| Index Case | Total No. | H/O Cancer Among Blood Relatives | | |
|---|---|---|---|---|
| | | Paternal only | Maternal only | Both |
| Male | 64 | 29 (45%) | 30 (47%) | 5 (8%) |
| Female | 46 | 15 (33%) | 28 (61%) | 3 (7%) |
| Total | 110 | 44 (40%) | 58 (53%) | 8 (7%) |

found to have 47% and 45% of relatives (50%) in maternal and paternal side respectively. Among female cancer patients with positive family history more maternal relatives (65%) were suffering from malignancy when compared to paternal relatives (35%) ($P < .05$).

Among the 154 patients various types of malignancy which constituted atleast four percent of cancer patients with positive family history were selected. Pharynx, Breast, Stomach, Cervix and Ovary were selected on this basis. Among these patients we tried to find out various sites of malignancy in their relatives. It is observed that the same site was affected by cancer in various generations, especially in cancers of the breast, stomach and cervix (Table IV). Of particular interest was breast cancer where six affected relatives of the twenty patients studied also had breast cancer. Seven of affected relatives of 22 cancer stomach patients had cancer of stomach and four of affected relatives of 12 patients with cancer cervix also had cancer of the cervix. But in ovary and pharynx only one of the affected relatives had the same type of cancer.

## DISCUSSION

Clustering of cancers in families has been reported in the literature[3,5,7]. This gives rise to the speculation that there may be a genetic component in the etiology of cancer[6]. Reported studies have shown an increased prediction for relatives of patients with leukaemias[6], carcinoma breast[3,4,5] and stomach[6] for the same or different types of cancer. Leukemias appear to alternate with solid tumours in alternate generation[6].

This study had attempted to describe these patterns. The numbers of individual cancers are too small to allow us to draw any firm conclusions. However, some facts emerged fairly strongly. Firstly familial history is reported in blood relatives of only four percent of all cancer patients. Curtis Mettlin et al[2] have reported family history of cancer in 13 percent of all first generation relatives and 15% in third generation relatives of patients with cancer. It is not known what proportion of patients with cancer gave familial history. It must be stressed here that our study relied only in history to document cancer among relatives. This is a weak evidence of cancer, however this was the best available. In a country where awareness is poor and coverage difficult, it is not practical to attempt to examine all relatives of patients with cancer before any meaningful pattern could be documented.

Another fact that emerged was that the highest prediction for familial occurrence was

**Table IV**

**Familial History of Cancer Patients Site and Their Blood Relative's Cancer Site**

| Blood Relatives Cancer Site | Cancer Patients' Site | | | | | | |
|---|---|---|---|---|---|---|---|
| | Pharynx (n = 12) | Breast (n = 20) | Stomach (n = 22) | Cervix (n = 12) | Ovary (n = 11) | Lymphatic (n = 12) | Others (n = 65) |
| 1. Pharynx | 1 | 1 | | | | | 6 |
| 2. Breast | 2 | 6 | 4 | | 2 | | 5 |
| 3. Stomach | 2 | 3 | 7 | - | 2 | 2 | 6 |
| 4. Cervix | 1 | 2 | 4 | 4 | 3 | 10 | 15 |
| 5. Ovary | | | | 1 | 1 | | |
| 6. Others | 8 | 8 | 8 | 8 | 4 | 8 | 65 |
| Total No. of Relatives Suffering From Cancer | 14 | 20 | 23 | 13 | 12 | 10 | 97 |

in cancers of the breast, cervix, colon and ovary. Less than five percent of patients with other types of cancer have given family history. This is also similar to findings in other series (1 to 8) were high proportions of affected relatives have been reported for these types of cancers.

A third factor is that maternal relatives rather than paternal relatives of female patients with cancer was seen to be more affected. No such pattern was seen for male patients with cancer. This findings does not appear to have been reported earlier.

Patients with certain types of cancer tended to have relatives with the same types of cancer. This was seen rather prominently in cancers of the breast, stomach and cervix where 30% were affected in each type of malignancy.

On examining the clustering of cancer sites in families it is evident that Breast and Stomach occupies an important position followed by cervix. Breast cancer patients have family members with Breast or stomach cancer and vice versa. Hence finding a case with stomach or breast cancer calls for screening of all the family members for the same site[2,8]. Since the same pattern is seen in the siblings, selective site screening for Breast or Stomach should be started at an younger age for individuals with family history of malignancy in stomach or breast. Male relatives of patients with gynaec cancer appear to be prone to develop cancer stomach, but female relatives appear to develop cancers of breast or cervix. This intriguing pattern does not seem to have been observed on other situations. Although this study is too preliminary for us to suggest that organised screening programmes should be initiated, the findings are interesting enough to warrant further study.

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