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ORIGINAL ARTICLE

Cancer Incidence in Married Couples

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Abstract

Background: Cancer among couples has been studied over several decades. In this article, the authors analyze the occurrence of cancer in couples having similar types of cancers in terms of histology, systems and organs based on the data collected.

Methods: The cancer data was obtained from a single US institution, from 2002 to 2017 from Tumor Registry. 13,255 analytical and 1,720 non-analytical cases were registered with cancer diagnosis. Cancer occurrence in different organs and systems between the couples was analyzed. Out of the 13,255 analytical cases, detailed analysis of 818 couples was conducted. The average age of participants at the time of diagnosis was 75 years for both spouses, and the median age was 76. Exploratory data analyses were conducted on types of cancers by systems and organs, as well as time of diagnosis of cancer between the couples and for spousal concordance.

Results: Historically, for cancer concordance between couples, the common factors like diet, smoking, alcohol, and environmental factors are given more credit than necessary as etiological factors. Even though, these factors remain common to couples, there is evidence for concordance in many types of cancers analyzed between couples as shown by this study. Especially, there was excess cancer concordance specific to organs like colon and rectum. The occurrence within days, weeks or months in the same site and organ between the couples raises plausible other causes than enumerated above.

Keywords

Spousal concordance, Cancer incidence, Data analysis

Introduction

Increased incidence of spousal cancers had been analyzed as early as 1955, 1961 and 1968 [1-3]. In specific cases studied in those articles, it was observed and remarked that cancer among couples had a higher incidence of spread for their partners, in comparison to the general population. Kyle and Greipp [4] report of two families in which successive spouses living in the same house develop multiple myeloma, which is a rare cancer to occur in couples. Occurrence of identical cancers in spouses, which is a rare phenomenon has been reported by many other authors [5-26]. In general, there is a definite increase in incidence of diverse types of cancers in spouses, that too occurring at an earlier age, possibly due to transmission between spouses.

General causes of cancer in the human population are ascribed to diet, smoking, hereditary/genetic, and environmental factors. The commonality of these factors may play a role in the causation of cancer in the spouses as well. Unrelated to the above factors, viruses have been identified as transmittal agents between spouses. For example, HPV related cervical, penile, oral and skin cancers, Hepatitis virus as factor causing Hepatoma, HIV infection causing human immune deficiency and associated lymphoma and leukemia, and finally, EB Virus causing lymphomas.

Specific to lung cancer unrelated to smoking, is the increased incidence of adenocarcinoma in general, and especially in spouses as suggested by McCarthy and Espiner [5]. Similar observation was noticed on concurrent cancer occurrence of melanoma among couples [5-8]. This raises suspicion to look for other causes in spousal cancers. Our study emphasizes similar observations that we will discuss in the subsequent sections.

Materials and Methods

We studied the cancer occurring in spouses over two

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separate time periods. Dr. Sarode Pundaleeka during his career as practicing oncologist spanning 36 years from 1981 to 2017, did initial analysis for the period of 1987 to 2001. The study included 10,498 patients diagnosed with cancer, of which a total number of 4,877 were males and 5,615 females. Details of the several types of cancer noted were as follows:

Breast Cancer: 1,974 cases,

Colon cancer: 933,

Prostate cancer 1,007, and

Lung Cancer 1,683.

Out of this total number of cases, there were 305 couples (Breast cancer: 105, Colon: 71, Prostate: 66 and Lung: 94 cases). The data was collected and not analyzed in detail or reported at that time. The observations prompted a compelling reason to understand the spread of cancer between couples. Then the second data was collected from 2002 to 2017 and detailed analysis was done. Current study is based on this second dataset.

This data includes 13,255 cancer cases. Out of these, the total number of couples diagnosed with cancer were 818. Details of the analyses are given in the next section.

Results

We analyzed the couples for their age correlations, sites of occurrence, and systems. Among the 818 husband-wife pairs studied, 194 pairs (23.72%) had diseases arising from the same system, remaining 624 (76.28%) had cancers arising from different systems (Table 1). Let us analyze the details in Table 1 by each system.

Digestive system

Digestive system cancer was found in 375 individuals. It occurred in 52 couples, 203 in males only, and 172 in females. From Facts and Figures 2015 data [27], the digestive system cancer rate for both sexes was 17.56%. In males it was 19.22%, and females it was 15.81%. In our data, the incidence rate was more than 5% in all the categories, namely, 24.82% in males, 21.03% in females and 22.92% in both sexes. The below Table 2 shows two parts, the GI cancers by each sex, and second part digestive cancers occurring in both couples.

Among the GI cancers (Table 2 first section), colon and rectal cases accounted for 71.2% in our data (134 males, 133 Females as shown in Table 2) compared to Facts and Figures [27] which showed only 45.57% of both sexes having colon and rectal cases in the digestive system. The occurrence of the cancer in the same location and diagnosed within days and weeks of the couples, is highly significant. This is explained in the Discussion Section. It raises the question of possible spousal transmission.

Table 1: Distribution of Cancer amongst 818 Husband and Wife Pairs.

		Wife								
Husband	**Digestive system**	**Endocrine system**	**Urinary system**	**Hematopoietic system**	**Lymphatic system**	**Reproductive system**	**Respiratory system**	**Other**	**Sum**
Digestive system	**52**	2	15	2	11	78	30	13	**203**
Endocrine system		**1**				4			**5**
Urinary system	17	1	**7**	4	5	39	17	2	**92**
Hematopoietic system	10	1	2	**1**	1	18	2	1	**36**
Lymphatic system	7		2	2		20	9		**40**
Reproductive system	39	1	11	4	9	**79**	26	9	**178**
Respiratory system	32	3	9	5	12	74	**54**	10	**199**
Other	15	4	6	2	3	24	10	1	**65**
Sum	**172**	**13**	**52**	**20**	**41**	**336**	**148**	**36**	**818**

Other: Skin, Brain, ENT, Unknown primary, etc

Table 2: Spousal digestive cancers by organ.

	Colon and Rectal		Wife						
Organ	**Males**	**Females**	**Husband**	**Cecum**	**Colon**	**Rectosigmoid**	**Rectum**	**Sigmoid**	**Sum**
Cecum	24	24	**Cecum**		1	1	1	2	**5**
Colon	34	48	**Colon**	1	3			1	**5**
Rectosigmoid	9	12	**Rectosigmoid**					1	**1**
Rectum	40	25	**Rectum**	1	5	1		2	**9**
Sigmoid	27	24	**Sigmoid**		2			2	**4**
Sum	**134**	**133**	**Sum**	**2**	**11**	**2**	**1**	**8**	**24**

Table 3: Spousal reproductive cancers by organ.

	Wife						
Male	**Breast**	**Cervix**	**Ovary**	**Uterus**	**Vaginal**	**Vulva**	**Sum**
Prostate	**51**	2	5	16	1	1	**76**
Scrotum	1						**1**
Testis	2						**2**
Sum	**54**	**2**	**5**	**16**	**1**	**1**	**79**

Table 4: Spousal respiratory cancers by organ.

Respiratory Cancers by Organ			Wife			
Organ	**Male**	**Female**	**Male**	**Larynx**	**Lung**	**Sum**
Larynx	14	7	**Larynx**		3	3
Lung	171	140	**Lung**	4	42	46
Pharynx	2		**Pharynx**		2	*2*
Pleura	10	1	**Pleura**		2	*2*
Other	2		**Other**			
Sum	**199**	**148**	**Sum**	**4**	**49**	**53**

Table 5: Spousal urinary system cancers by organ.

	Wife		
Husband	**Bladder**	**Kidney**	**Sum**
Bladder	1	4	5
Kidney	1	1	2
Sum	**2**	**5**	**7**

Reproductive system

In our study, the highest number of cancers in the spouses occurred in the reproductive system. 514 (336 females and males 178) individuals had reproductive cancers amounting to 28%. Among those 336 cases in females, most cancers occurred in breast, uterine, cervical, and ovarian accounting to 330 cases. In males, majority of them had prostate cancer, 174 out of 178. In females the breast, cervix, ovary was accounting for 33.74%. In Males prostate cancer accounted for 21.27% of the total number of cases. From Facts and Figures [27], the total number of the reproductive system cancers was 33.98% of the total number of cases, higher than case study data. 79 couples had both reproductive cancers as shown in Table 3.

Further analysis in Table 3 presents the interrelation between the reproductive cancer among the 79 couples. 51 cases had wife with breast cancer and husband with prostate cancer. 21 of the women with uterus and ovarian cancer, their spouses all had prostate cancer. Average age was 74 years for men with prostate and their wives having breast cancer had the average age 72 years. 3 of the couples were diagnosed with cancer within 10 days of each other! The prostate cancer in men associated with cancer of the uterus, ovary and cervix in women occurred at the average age of 73 and 72 years respectively, and 4 cases were diagnosed within two months of each other. These are intriguing observations and exceedingly difficult to explain the reason.

Respiratory system

347 spouses had respiratory cancers (18.9%). We analyzed respiratory cancers by their organs of occurrence within each sex. Table 4 contains two parts, first one of respiratory cancers by each sex; and second part, contains both couples having respiratory cancers.

In the respiratory system, lung cancer patients were 140 in females and 171 in males as shown in Table 4, totaling 311 lung cancer patients which amounted to 89.6% of the total respiratory cancers. Compared to Facts and Figures 2015 [27] occurrence is at 92%, our data is showing lesser respiratory cases. In men

with lung cancer, adenocarcinoma was found to be 29.23% (50 out of 171) and squamous cell carcinoma was 26.31% (45 out of 171). Similarly, in women with lung cancer, adenocarcinoma accounted for 37.85% (53 out of 140), and squamous cell carcinoma 15.7% (22 out of 140). Squamous cell carcinoma incidence is higher in men compared to women, can be explained by increased incidence of smoking in men compared to women. Adenocarcinoma incidence in women which is higher than in men is difficult to explain. Among the 53 couples both diagnosed with cancer in the respiratory system, 42 pairs both spouses had lung cancer (Table 4 second section). Among the lung cancer cases in the spouses of 311, small cell/oat cancer accounted for 19.93%, squamous cell 21.54%, and adenocarcinoma accounted for 33.12%. With both spouses having lung cancer in the 42 couples, we could not identify any specific histology that was predominant.

Urinary system

For the urinary system by organs, there were more bladder and kidney cancers. There were 7 cases of both couples affected with kidney and bladder cancers as shown in Table 5.

In one of the couples with urinary system cancer both husband and wife were diagnosed with transitional cell carcinoma *in situ* of the bladder within 148 days of each other. Second couple wife had the transitional cell carcinoma of the renal pelvis and the husband transitional cell cancer of the lateral bladder wall. In the couple with both kidney cancer, the male was diagnosed with renal cell carcinoma and female with squamous cell carcinoma of the kidney. Among the 4 couples with husband bladder cancer and wife kidney cancer, for one couple the male had papillary transitional carcinoma of the bladder, while the female had transitional cell carcinoma of the renal pelvis. Three other couples with female kidney cancers, one female had renal cell and other two had clear cell carcinoma. Their male spouses all of them had transitional cell carcinoma of the bladder.

Age distribution analysis

Median age was 76 years for both husbands and wives, their average age 75 at the time of diagnosis. Age distribution between the males and females was similar, incidence peaked in the range of 70 to 79. However, there are many outliers (age above 100 in some cases), when evaluated for normality using Shapiro-Wilk test, the p-value is much below 0.05, indicating compelling evidence of non-normality. All individuals were of age later than 30 years. We inferred on an average that a spouse developed cancer at the similar age range as his/her partner. This we evaluated using the null hypothesis that there is no difference between age distribution of both sexes and had no evidence to reject that null. However, the time difference of cancer occurrence between the couples varied over from few days to years. Unlike other reports reporting cancer occurring in couples at a lower age overall, our study showed the age at diagnosis was higher.

Compared to the Cancer Incidence data in US (breast cancer median age is 63, prostate cancer median age 66), we find that the couples with cancer had a median age of 75 for breast cancer, and 77 for prostate cancer. This data is skewed towards the higher median age, due to couples in our study were diagnosed with cancer at later age 77-79 years.

Next, we analyzed the age difference based on the time of diagnosis between the couples. It varied from few days to years depending on the types of cancer. We had noticed that in 69% of the cases, couples developed cancer within 7 years from the time one of the spouses got diagnosed. Figure 1 below shows the yearly total of spousal concordance time difference.

It shows 20.29% of spousal cancer developing within one year. Further, one can notice that highest total of cancer occurring between spouses is within one year!

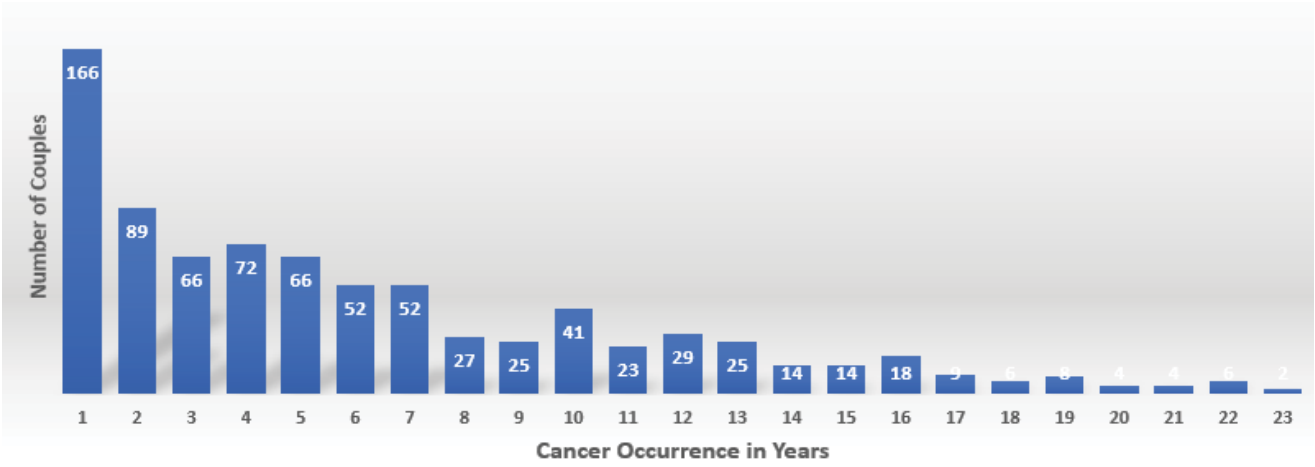

Figure 1: Cancer occurrence time difference between couples in years.

Discussion

The incidence of cancer among spouses was analyzed based on data collected over 15 years from a single institution in US. Since substantial concordance within couples were found, suggesting screening tests and/or procedures should be instituted in non-affected spouse as soon as the diagnosis is established, as the cancers occurred in the same system or even organs analyzed for the spouses. Among the 818 couples studied, 194 pairs (23.72%) had diseases arising from the same organ/system, and the remaining 624 (76.29%) had cancers arising from different organs or systems. The dominant organ/system of spousal concordance was noticed in the reproductive (79 pairs, 9.66%), respiratory (54 pairs, 6.6%), and digestive (52 pairs, 6.36%) areas. Even though respiratory system has identifiable causes, viz., smoking, the other two systems there is no single factor ascribed so far.

Data regarding the incidence of colon and rectal cancer occurring in both spouses in specific population from China as reported in Liu, et al. [28] from NCCR data, was 10.73% for both sexes, 10.65% for men and 10.82% for women. Same data for general population in USA obtained from Facts and Figures [27] showed incidence of 8% in both sexes, 8.1% for male and 7.85% for female. In our study, a total 267 colon and rectal cancers were found in the spouses. This amounts to 16.32% both sexes, 16.38% in males and 16.26% females. This shows a significant increase in the colon and rectal cancer incidence in the spouses. We see the doubling of colon and rectum cancer in the married couples living together compared to general population [29].

Among the lung cancers, 41.48% were due to pure squamous cell (21.54%) and small/oat cells (19.94%). This can be ascribed to smoking and possibly environmental factors too. However, it is difficult to explain the cause for 58.52% of the other histologies. Especially, it becomes challenging to explain the adenocarcinomas accounted for 33.12% of the cases in both spouses, more than other histologies. Adenocarcinoma of the lung is increasing, while smoking incidence and prevalence is decreasing in US Population [27].

Regarding reproductive system cancers, the most common is prostate in men and breast cancer in women. Compared to cancer incidence data in US [27] (breast cancer development is median age of 63, prostate cancer median age 66) in our study we find in the couple, women developed breast cancer at the median age of 75 and men developed prostate cancer at the age of 77. This delay of 12 years in women, and 11 years in men is fascinating and unexplainable. Still noteworthy, all the cancers in reproductive systems starting with breast, ovarian, endometrial cancer in women and prostate cancer in men are all adenocarcinomas. To date, there is no cause attributed or speculated for etiology of adenocarcinoma. Is there a transmitting agent, especially among spouses?

Further, our specific observations with respect to individual couples are as follows:

- Single couple cases both having cancer occurring in the same organ/system:
  - Bladder carcinoma *in situ* of the bladder diagnosed within 5 months of each other.
  - Multiple myeloma within 43 days of each other.
  - Adenocarcinoma of the head of the pancreas for both diagnosed within 274 days.
  - Signet ring cell carcinoma of the stomach, even though the diagnosis timing was approximately 10 years between the couple.
  - Pituitary adenoma diagnosed in both spouses within 22 days.
  - Bronchoalveolar carcinoma diagnosed in both couples.
- Colon cancer in 3 couples:
  - First couple both with ascending colon cancer diagnosed within 5 days of each other.
  - Second couple both with hepatic flexure and carcinoma diagnosed within 29 days of each other.
  - Third couple, both had adenocarcinoma *in situ*, husband in hepatic flexure and wife in transverse colon within 123 days.
- Sigmoid colon cancer among two couples:
  - One of them carcinoma *in situ* diagnosed within 4 days,
  - Other couple with invasive adenocarcinoma was identified within 74 days.

These short durations of cancer occurrence in the similar location raises the question regarding the question of causative factor in colon cancers.

Proven cause of epidermal cancers in spouses is the Human Papilloma Virus (HPV) [30]. This is an epidermal/skin/ectodermal tropic virus. This affects the vulva, vaginal and cervix in women. In men, it affects the penis and scrotum. Of late, more of the cancers related to HPV affect oral cavity in both sexes depending on the sexual activity preferences. HPV is transmitted through close contacts, sexual or otherwise. This is dependent on the viral factors such as different strains occurring in different geographical locations. In addition, the host factors will be age, sexual predispositions, nutritional, and immunological statuses. For cancers occurring in similar organs, Kim, et al. [15] reported 3 cases in 1982:

- Two couples with nodular NHL and one couple with large cell lymphoma.

- Non-Hodgkin's lymphoma 5 to 8 years apart between the couples.

When this paper was published, the etiology EB virus causing non-Hodgkin's lymphoma was not established. But the authors speculated a transmissible agent. Our study further provides data, for a possible transmissible agent between couples for other cancers.

We also hypothesize that there are possible tropic viruses causing adenocarcinoma in various organs arising from the mucous glands due to the transmissible agents between spouses. Mucous glands are present universally in the body. The HPV virus tropic to epidermal cells causes cancer wherever epidermal cells are present [30].

Conclusion

There have been multiple case reports and published data on cancers developing in couples. Current study based on 15 years of data collected from a single US institution further strongly emphasizes possible etiological factors for spousal concordance. Among the 818 couples studied, 194 pairs (23.71%) had diseases arising from the same organ/system. We notice more than 5% increase in the digestive system cancer among the couples compared to the general statistics [27,31]. We have analyzed the spousal cancer occurrence at the system and organ level, that too developing within brief period after the other partner was diagnosed. It not only suggests screening of spouse as soon as possible, but also identify causal factors.

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Conflicts of Interest

None.

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