

Full Length Research paper

Prevalence of breast cancer in menopausal blind women

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A correlation between prevalence of breast cancer with blindness has not been attempted in India and only scanty information is available at the world scenario as well. We have done a pilot study by epidemiological survey of blind menopausal (high risk age group) women (n = 204) from Chennai to find the prevalence of the disease. In the present study, menopausal visually challenged women have shown that the ratio at risk of developing breast cancer in this group is very much lower (1:100) compared to sighted women in the similar age group, The risk of developing breast cancer is 1:78 (Cumulative Risk 35 - 64 age), among sighted women in Chennai. Statistical analysis of the present data also provide enough evidence that blind women who are > 40 years of age had 13% greater risk of breast cancer compared with those in the study group < 40 years (RR = 1.125; 95% CI = 0.07 to 17.74).The susceptibility to develop the disease among partially blind women is almost twice than that of totally blind women (RR = 2.14; 95% CI = 0.14 to 33.68). Similarly menopausal stage of a woman has more risk of developing breast cancer than pre-menopausal stage (RR = 5.18; 95% CI = 0.33 to 80.75). Vision loss after menarche also indicates an increased risk (RR = 8.27; 95% CI = 0.54 to 127.6).The intervals for these risks give a very wide range of possible values for the corresponding risk ratio due to small sample size and the rarity of breast cancer among blind women. The topographical location of India close to the equator and life style pattern of the people could be the major reasons for the very low prevalence of breast cancer in Chennai. None of the other high or low risk factors were found to be influencing blind women to develop breast cancer. The relationship between visible light and breast cancer can be studied by taking blind menopausal women as a model.

Key words: Blindness, breast cancer, epidemiology.

INTRODUCTION

Blue light is being identified as a new environmental pollutant. Earlier we studied the effects of day light in anophthalmic rats and concluded that the mammalian eye sub serves at least two photic systems: the occipital cortex, which mediates the conscious perception of light and recognition of images and a subcortical system that med-iates light-sensitive synchronization of the circadian pace-maker (Foster et al., 1991; Chaurasia and Gupta, 1999; Jagota et al., 1999).

The clock-cancer connection has been proved from investigations involving pilots, female flight attendants and shift workers who are more likely to have disrupted circadian cycles due to abnormal working hours in different

different parts of the world. Artificial light at night disrupting the natural melatonin- estrogen balance was linked with the increase in hormone regulated breast cancer among women (Pukkala et al., 1995; Tynes et al., 1996; Hansen, 2001 a, b; Pukkala et al., 2003; Hansen, 2006; Davis and Mirick, 2006; Schernmmer et al., 2006; Franzese and Nigri, 2007; Viswanathan et al., 2007). Blind women follow natural system of rhythm due to lack of light through eyes. Blast et al. (2005) have established that increase in melatonin levels causes the suppression of tumor growth *in-vivo* in nude mice model.

The literature survey showed very scanty information on the prevalence of breast cancer in blind women world-wide. The first preliminary evidence linking light to cancer in people emerged from the register based studies of Hahn (1991). He computed the incidence of this malignancy in blind and sighted women and discussed

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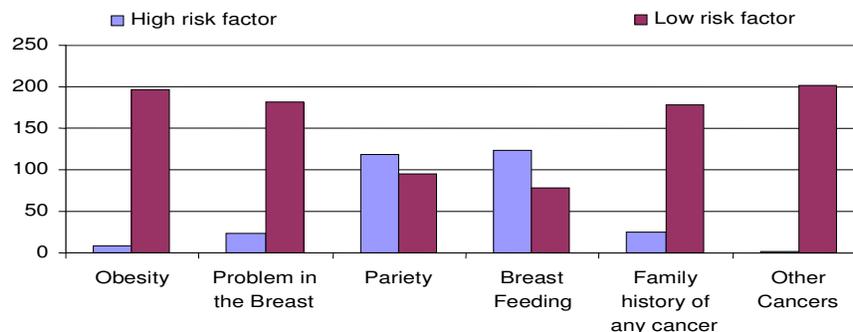


Figure 1. Prevailing ratio of established risk factors observed among study subjects.

the connection between light and melatonin in visually impaired women. As early as 1990, scientists reasoned that anybody whose eye cannot detect light should be resistant to estrogen generated tumors. This angle of discussion paved way for the epidemiologist to reason that people whose eyes can not detect light should prove resistant to tumor growth. Subsequently, Feychting et al. (1998) and Verkasalo et al. (1999) supported melatonin hypothesis from their studies based on cancer registry in Sweden and Finland respectively.

The later found 50% decreased risk of the disease and an inverse association between breast cancer incidence and degree of visual impairment. Similarly, Kliukiene (2001) found only 5 subjects suffering from breast cancer among 15,412 visually impaired subjects in Blind Registry in Norway. Pukkala et al. (1999; 2006), added to the suggestive epidemiological evidence for the 40% decreased risk of hormone related cancers in people with visual impairment and consequently established a relationship between exposure of visible light at night and breast cancer risk in Finland.

The hypothesis is further advanced that blindness from an early age may lead to a further reduced risk of breast cancer through altered patterns of melatonin secretion by the pineal gland. The effect of age at the onset, duration and degree of blindness could also be assessed after adjustment for known risk factors for breast cancer (Coleman and Reiter, 1998).

India is the home to one of the world's largest population (12 million suffering from visual impairment, Census of India, 2001). The literature survey did not show any published data on visually impaired adult menopausal women suffering from breast cancer in India. We are interested to have data on breast cancer among visually impaired menopausal women in the Indian population, therefore, a pilot epidemiological survey was undertaken to establish the prevalence of breast cancer among visually impaired menopausal women in Chennai.

MATERIALS AND METHODS

This study included menopausal women with visual impairment

registered in governmental and non-governmental rehabilitation centers as well as MMTR (Madras Metropolitan Tumor Registry) during June, 2006 – June, 2007. Since national registry for the blind is not available, these three sources of information helped in the present epidemiological survey.

In the present study, data were obtained from personal communication with the study population of women as well as from the cancer registry. For ascertaining the degree of visual impairment (total blindness and partial blindness) a manual of classification of impairments, disabilities and handicaps, WHO Geneva, (1980) was used. The data on the risk of developing cancer among normally sighted women was procured as courtesy from MMTR 2003 - 2005 for comparison. Special care is taken to prepare a proforma for recording the data (Sample is enclosed). Only blind women menopausal age (30 - 40) and post menopausal age as above 40 (risk age) were considered for the present study. Women having menstrual cycle after 40 years are also included as pre-menopausal stage. Statistical software Epi - Info (2005) was used to analyze the data.

RESULTS

Chennai is situated at the sea level on the East coast of India. It lies between 12° 9' and 13° 9' of the northern latitude and 80° 12' and 80° 19' of the Southern longitude spreading in 178.20 km² area.

In the survey out of 204 (collected during 2006 - 2008) menopausal blind women, we found only two subjects suffering with breast cancer. The cancer was operated at appropriate time and the subjects are now leading a normal life until December, 2008.

"Well established" high risk factors for prevalence of breast cancer such as obesity, problem in the breast, parity, breast feeding, age of the first pregnancy, family history of any cancer (genetic), age, suffering from other cancers and suspected risk factors such as partial blindness, late menopause (beyond 45 years) and age of onset of blindness (before or after menarche) were also considered for the analysis to find how many are at risk of developing breast cancer in addition to their age (Figure 1).

The ratio of "well established" high risk factors for prevalence of breast cancer such as, obesity, problem in breast tissue, nulliparity, not breast fed, age of the first pregnancy (above 35 years of age), family history of any

Table 1. Observed frequencies for determining risk ratio or relative risk.

	Disease present	Disease absent	Total
Exposed to factor	a	b	a+b
Unexposed to factor	c	d	c+d
Total	a+c	b+d	n = a+b+c+d

cancer and those already suffering from other types of cancer observed among the study group is represented in the bar chart in Figure 1.

High risk factors

Obese, problem in the breast, no parity, not breast fed, having family history of cancer, prevalence of other cancers.

Low risk factors

No problem in the breast, parity, breast fed, no family history of cancer, absence of other cancers.

Among the study subjects 4% were obese, 11.27% suffer from other problems in the breast tissue. 60.78% did not feed their children and 14.22% show nulliparity. 12.25% had the first child above 35 years old (late pregnancy) and 12.25% have family history of cancer. In addition, suspected risk factors such as late menopause (16.2%), partial blindness (31.86%) and age of onset of blindness (after menarche) (10.78%) were also recorded. Even though these risk factors were observed, among the study group only two had breast cancer. Among those, one is forty five years old (in 2007), weaver, suffers from total blindness, lost her vision when she was 13 days old baby, unmarried, attained menarche at the age of 13 and is in menopause now and the other one is thirty seven years old (in 2007) partially blind, homemaker, unmarried, attained menarche at the age of 12 (early menarche) and is in pre-menopausal stage now.

Statistical analyses

Relative risk (RR) was used as a measure of association between risk factors and susceptibility to develop breast cancer in women; the RR was defined as the ratio of the risk of developing a disease among those exposed to a specified risk to those not exposed to this risk. The 95% confidence intervals (CI) for these relative risks were also calculated.

The risk ratio or relative risk (RR) is used to find the association between a disease and a possible risk factor. The observed frequencies are given in Table 1. RR is calculated thus:

$$\text{Estimated relative risk (RR)} = \frac{\text{Estimated risk in the exposed group}}{\text{Estimated risk in the unexposed group}} = \frac{a/(a+b)}{c/(c+d)}$$

The 95% confidence interval for the true population, *ln* RR is given by:

(*ln* RR - 1.96* SE (*ln* RR)) to (*ln* RR + 1.96* SE (*ln* RR)) and the standard error (SE) of *ln* RR is given by:

$$\text{SE} (\ln \text{RR}) = \sqrt{\frac{1}{a} - \frac{1}{a+b} + \frac{1}{c} - \frac{1}{c+d}}$$

Antilog (e^x) of these lower and upper limits in order gives the 95% confidence interval for the population relative risk.

Statistical analyses of the data also provide enough evidence that blind women who are > 40 years of age had 13% greater risk of breast cancer compared with those in the study group < 40 years (RR = 1.125; 95% CI = 0.07 to 17.74) in our study. The susceptibility to develop the disease among partially blind women is almost twice than that of totally blind women (RR = 2.14; 95% CI = 0.14 to 33.68). Similarly postmenopausal stage of a woman has more risk of developing breast cancer than pre-menopausal stage (RR = 5.18; 95% CI = 0.33 to 80.75). Vision loss after menarche also indicates an increased risk (RR = 8.27; 95% CI = 0.54 to 127.6).

The intervals for these relative risks give a very wide range of possible values for the corresponding risk ratio may be due to the small sample size and the rarity of breast cancer among blind women.

DISCUSSION

Breast cancer is the leading cause of death in women all over the world. According to the report of World Health Organization (WHO) 519, 000 deaths occur every year worldwide (WHO, 2009).

Studies indicate that due to changed life style in India increasing rate of breast cancer is quite alarming. Now, it is second most common malignancy in Indian women (Yeole and Kurkure, 2003). During 2005, study conducted by the International Association of Cancer Research, based in Lyon, France, projected that there would be 250, 000 cases of breast cancer in India by 2015, a 3%

increase per year. Currently, India reports roughly 100,000 new breast cancer cases annually though a significant regional variations in incidence rates persists. The overall rate is now estimated at 80 new cases per 100,000 population per year (Bagchi, 2008). According to an Indian health News report one in 22 women in India are likely to suffer from breast cancer during their lifetime, while the figure is definitely more in America with one in eight being a victim of this cancer. Breast cancer incidence had zoomed by 200% since 1982. The three-and-half-year-long study was initiated after the number of breast cancer cases exceeded that of cervical cancer in the Madras Metropolitan Tumor Registry in 2003. In Chennai, the most common cancer among women relates to the breast and though the incidence is 50% lower in rural areas, it has been steadily increasing. Women above 30 years of age are the most likely to get cancer (Shantha et al., 2003).

This pilot epidemiological study is the first attempt to collect scientific data on blind menopausal women with respect to breast cancer. No studies have been done in India earlier to find neither prevalence nor incidence rate of breast cancer in blind women. Comparison of the present data is not possible with existing observations of the register based studies from Scandinavian countries due to lack of registry for blind subjects in India.

In the present study, visually challenged menopausal women has shown the risk of developing breast cancer in life time is very much lower 1:100 ($n = 204$) since, only two suffered from the disease among our study group. However, Shantha et al. (2008) showed that the risk of developing breast cancer among sighted women in Chennai is 1:78 (Cumulative Risk 35 - 64 age).

Feychting et al. (1998) supported melatonin hypothesis with the cohort study consisting of 1,567 totally blind and 13,292 severely visually impaired subjects from Swedish cancer registry and found that blind people have a lower cancer incidence. Similarly, Verkasalo et al. (1999) also found 50% decrease in the risk of developing the disease. They also showed an inverse association between breast cancer incidence and degree of visual impairment from cancer registry in Finland. The health survey data from the cancer registry of Norwegian government had approximately 15,412 visually impaired entries. Among them only 5 subjects suffered from breast cancer (Kliukiene, 2001).

Subsequently, Pukkala et al. (1999; 2006), from a cohort study consisting of people with visual impairment identified from Finnish cancer registry for years 1983 - 2003 added to the suggestive epidemiological evidence for the decreased risk of hormone related cancers in people with visual impairment. The cohort consisted of 17,557 of persons with visual impairment (11,147 women, 6,410 men) showing only 184 cases of breast cancer, which represented a 40% decrease in the risk of developing breast cancer and established a relationship between visible light at night and breast cancer risk.

Due to the topographical location of India (being close

to the equator), having almost 12 h light and dark cycle, unlike the Scandinavian countries, having long day / night periods due to the location close to the poles. Image forming photic receptors are absent in blinds but photic receptors for synchronization of circadian rhythms are present in visually impaired subjects. Therefore, they maintain a natural and normal circadian rhythm Jagota et al. (1999). However, the photic reception which is responsible for perception of light is lacking in blind women and so they may become less prone to breast cancer. In the Indian scenario circadian rhythms are more stable than Scandinavian countries and this could be the major reason for the very low prevalence of breast cancer reported compared to the Scandinavian countries in this study.

Other reasons for low prevalence of breast cancer in Indian blind population may be due to their abstinence from smoking (Gammon et al., 2004), alcohol and under taking vigorous physical activity compared to Scandinavian population (Detailed Guide: Breast Cancer, 2008). In the present investigation among our study group 60.78% did not feed their children and 14.22% showed nulliparity, 12.25% had their first child above 35 years old (late pregnancy) showing that they fall under "well established" risk factors (Barnett et al., 2006; Goodwin, 2008; Travis et al., 2006) for developing breast cancer however, these risk factors did not show much effect on blind population, nevertheless these account for 50 - 55% of the breast cancer risk among Westernized populations.

Similarly, single women and nulliparous married women were prone to the disease approximately 1.4 times more than that of parous married women. The published data showed that, women who breast fed their infants had a 17% lower risk of breast cancer compared to women who did not breast fed (Hendry, 2008). Women whose first child was born before they were 20 years of age had approximately less 50% risk of developing breast cancer than women whose first birth was at age 30 years (Leslie Bernstein et al., 2003). Among the study subjects 12.25% have family history of cancer. About 5 to 10% of breast cancer cases world wide are thought to be hereditary, resulting directly from gene mutations, inherited from a parent(s). Altogether, about 20 to 30% of women with breast cancer have a family member with this disease (Detailed Guide: Breast Cancer, 2008; Gajalakshmi et al., 1998). In addition, suspected risk factors such as, obesity (4%), other problems in the breast tissue (11.27%), late menopause (16.2%), partial blindness (31.86%) and age at onset of blindness (after menarche) (10.78%) were also recorded. It has been calculated that women with menopause at each 5 year age difference have 17% higher risk of breast cancer (Hsieh et al., 2006).

It is surprising that the above discussed risk factors seem to be either non-operative or suppressed in blind menopausal women to develop the disease. However in the two breast cancer cases the risk factors such as nulliparity, not breast fed, early menarche and partial

blindness (case-I) could be the contributory factor of the cancer susceptibility genes such as P53, BRCA I and BRCA II etc. (Detailed Guide: Breast Cancer, 2008). No other obvious reasons can be assigned to these two cases for developing breast cancer in the present study. Encouraged with this data we have extended our study to the whole province of Tamil Nadu with the population 62, 405, 679 including 964, 063 visually handicapped subjects.

Conclusion

The result of the present study is an additional epidemiological evidence suggesting a relationship between visible light and breast cancer risk. However, little is known about possible molecular mechanisms underlying this clock-cancer connection. So, further study at the molecular level is very essential to confirm the reason for the very low prevalence of breast cancer in the Indian scenario.

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APPENDIX

INCIDENCE OF BREAST CANCER IN BLIND WOMEN EPIDEMIDLOGICAL STUDIES

Proforma 1.

- (A)
- 1 Project area: Eye research
 - 2 Organization undertaking the project -----
 - 3 Name of field worker: -----
 - 4 Name of village: -----
 - 5 Taluka and District: -----
 - 6 Date of survey: -----

- (B)
1. Name of the subject: -----
 2. Address: -----
 3. Date of birth and age: -----
 4. Type of blindness: Total ----- Partial -----
 5. Occupation: -----
 6. Cast / Religion: -----
 7. Marital status: Married----- Unmarried -----
 8. Age of marriage: -----
 9. Issues: Age of first pregnancy: -----
 Age of second pregnancy: -----
 Age of third pregnancy: -----
 10. Miscarriages / Abortions: Yes ----- No -----
 11. Breast feeding the baby: Yes ----- No -----
 If "No" why: -----
 12. Have you any problem in breast: (A) Lump ----- (B) Pain ----- (C) Any other –
 13. Any family history of breast cancer: (A) Grandmother ----- (B) Mother -----
 (C) Mother's sister ----- (D) Sister -----

Proforma 2.

1. Food habits : Vegetarian ----- Non-vegetarian -----
2. Physical status : Obese ----- Normal ----- week -----
3. Socioeconomic condition : Higher Middle ----- Middle -----
 Lower Middle class -----
4. Age of menarchy: -----
5. Age of menopause: -----
6. Age of acquirement of blindness: -----

7. Reason of blindness : Accidental ----- Disease ----- Congenital -----
8. Any other disease : Which -----
 From when -----
9. Gynecological disease : -----
10. Regularity of cycle: -----
11. Have you taken any steroid medicine: Yes/No, if Yes Which -----
12. Any Diagnosis/ Advise/ Treatment from doctor regarding the breast problem:-----