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PSYCHOLOGICAL ISSUES AMONG PATIENTS WITH HEREDITARY CANCER AND THEIR FIRST-DEGREE RELATIVES VISITING A TERTIARY CARE HOSPITAL IN INDIA

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Abstract

Cancer susceptibility is higher among those with a family history. Still, nationally, clinical genetic services and the psychological impact of suspected familial cancer on patients and relatives remains a budding field. It also remains unclear if genetic testing and counseling (GTC) can help in alleviating common psychological issues associated with cancer. This research effort analyzed the association between GTC and psychological issues including, anxiety, depression, and distress among patients with hereditary cancers and their first-degree relatives. This pilot effort enrolled 100 patients visiting the GTC center at All India Institute of Medical Sciences and their relatives. At baseline and post GTC, demographic information was obtained, and psychological issues of interest were assessed using validated questionnaires. Generalized estimating equations accounting for within-person clustering were used to analyze the association between GTC and the three psychological issues of interest. Of the total 96 of the patients were females, and 60% and 26% respectively had breast and ovarian cancer. Among patients, as compared to pre-GTC post-GTC, the cancer type and age adjusted odds of having anxiety, depression, and distress were lower. These estimates were significant for distress (OR: 0.37; 95% CI: 0.21, 0.68). Among relatives, although insignificant, GTC resulted in a 40% reduction in distress (0.60; 0.29, 1.24). Our results provide preliminary support to potential protective effect of GTC among cancer patients and their first-degree relatives for psychological distress related to the condition. A confirmatory future larger longitudinal study analyzing these association is recommended.

***Keywords**: Hereditary Cancer, Psychological issues regarding cancer, Genetic Testing for patient relative.*

INTRODUCTION

Cancer, characterized by the uncontrolled growth and spread of abnormal cells, is a group of diseases that causes one in seven deaths worldwide[1-2]. In low- and middle-income countries, it is the third leading cause of death after cardiovascular diseases, infectious, and parasitic diseases. It is now known that for most cancer cases, susceptibility is higher among those with a family history. While many familial cancers result from an interaction of genetic and environmental factors; some are strictly a result of inherited genetic alteration or mutation[1-2]. Inherited genetic mutation play a major role in about 5 to 10 percent of all cancers[3]. In the past decade, several hereditary cancer syndromes have been described including familial adenomatous polyposis, hereditary breast and ovarian cancer syndrome due to BRCA 1/2 mutations, hereditary non-polyposis colorectal cancer, and Li Fraumeni syndrome[3]. Anxiety and depression related symptoms, with a prevalence of

around 50% among cancer patients and their relatives are common psychological issues that negatively affect the lives of the patients and their families[4]. Relatives often report severe emotional distress, significant fatigue, sleep impairment, and difficulty maintaining their focus and energy throughout the cancer treatment process of their loved ones; many symptoms of which characterize depression[5]. In the year 2012, 14.1 million new cancer cases excluding non-melanoma skin cancers were reported worldwide; of which 57% (8 million) occurred in economically developing countries[6]. In India specifically, over 1 million new cancer cases are reported every year. In the same year, an estimated number of 600,000-700,000 cancer-related deaths were recorded[6]. As of 2018, there were an estimated 18 million cancer cases in the world with lung and breast cancer, a hereditary type cancer being the most common cancer types[7]. Still, clinical genetic services and the psychological impact of suspected familial cancer on patients and relatives remains a budding field with only a couple centers offering such services[8]. Due to the inherent complexities in communication genetic risk related information, it is still unclear how well is the former understood. It is also therefore unclear if genetic counselling can help in alleviating psychological issues like anxiety, depression, and distress[9]. To bridge this gap between such suspected familial cancer and need-based genetic testing and counselling (GTC), we have established one such center at the All India Institute of Medical Sciences (AIIMS), the premier most medical institute in the country. This center coordinates with Oncology OPDs from where patients are now being referred to this center. This paper explores the impact of the diagnosis or suspicion of familial cancer on the psychological stress, anxiety, and depression among patients and their relatives.

METHODS

Sample and setting: The study sample consisted of patients with hereditary type of cancers and their first degree relatives. The study participants were primarily enrolled either referred to the newly established GTC center at AIIMS, by the treating physician. Some participants were enrolled after they visited the center after finding about it from the pamphlets placed within AIIMS. To be eligible to participate, the participants had to be at least 18 years of age and provide informed consent to enroll in the study. Those with previous history of mental health disorders were excluded from this study. The intended sample size for this pilot project was 100 patients and relatives each. This was based on the estimates produced by previous research efforts. This effort was able to enroll 100 patients and 52 first degree relatives in the final study sample.

Variables: At baseline, demographic,and cancer and its treatment-related information (name, age, gender, religion, marital status, education, occupation, residential address, cancer type, and cancer-treatment related information) was obtained. The psychological issues of interest i.e. anxiety, depression, and distress were respectively assessed using three pre-validated questionnaires i.e. Generalized Anxiety Disorder (GAD)-7[10], Patient Health Questionnaire (PHQ)-9[11], and Distress Thermometer (DT) [12], each of which obtained information on a Likert scale. Post-counselling, the psychological issues were re-assessed after one month using the same tools.Anxiety and depression wereeventually coded as ‘no’ if the levels reported were less than five and ‘yes’ if these were equal to or greater than five. Distress was coded as ‘no’ if it lied between zero and three and ‘yes’ if it was equal to four or greater. This was done because of the low cell counts.

Analysis: Descriptive statistics (frequencies and percentages) for the study exposures within each

of the outcomes of interest are provided. The crude and multivariable analysis compared the outcomes of interest in the post-counselling phase as compared to pre-counselling. The multivariable models were adjusted for cancer type and age. Generalized estimating equations accounting for within-person clustering and with independent working correlation matrix were used. Note that for the regression models, the analyses were only limited to the two hereditary cancers i.e. breast and ovary.

All analyses were conducted in SAS statistical software[13].

RESULTS

Table-1 shows the respective proportion of participants with the psychological issues of interest before and after counselling for each of the study characteristics. In general, as compared to the respective proportion before, after counselling the proportion of adults with the psychological issues i.e. anxiety, depression, and distress were lower. However, the proportions varied by the characteristic under consideration as shown in **Table-1**.

Table-2 shows that among the 52 first degree relatives,again, in general we observed a reduction in the proportion of respondents who had the psychological issues after counselling as compared to the proportion who had the former before counselling. For example,among those with anxiety before counselling, 43%, while post counselling, the proportion of females with anxiety was 36%. On the other hand, among those with anxiety in the pre and post-counselling phase respectively, 57% and 64% were males. The proportions also varied by cancer type with those with accompanying a patient with breast cancer having lower proportion of psychological issues after counselling and those with ovarian cancer having higher proportions.

Chi-squared tests revealed that overall, there was a significant difference in the outcomes between and pre- and post-genetic counselling proportions (P<0.05) among patients. Among relatives, there was significant difference among the former for depression and distress, but not anxiety (p=0.06).

Table-1: Frequencies and proportions of patients across demographic and cancer-related characteristics by the psychological outcomes of interest (n=100)

Characteristics	Psychological outcomes of interest n(column %)												
	Pre-test anxiety		Post-test anxiety		Pre-test depression		Post-test depression		Pre-test DT		Post-test DT		Total
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	
Gender													
24 (92.3)	72 (97.3)	30 (88.2)	59 (100.0)	23 (95.8)	73 (96.1)	32 (88.9)	57 (100.0)	18 (90.0)	78 (97.5)	36 (92.3)	53 (98.2)		
2 (7.7)	2 (2.7)	4 (11.8)	0 (0.0)	1 (4.2)	3 (4.0)	4 (11.1)	0 (0.0)	2 (10.0)	2 (2.5)	3 (7.7)	1 (1.9)		
Religion													
Hindu	20 (76.9)	64 (86.5)	28 (82.4)	50 (84.8)	19 (79.2)	65 (85.5)	29 (80.6)	49 (86.0)	16 (80.0)	68 (85.0)	34 (87.2)	44 (81.4)	
Others	6 (23.1)	9 (12.2)	6 (17.6)	8 (13.6)	5 (20.8)	10 (13.2)	7 (19.4)	7 (12.3)	4 (20.0)	11 (13.8)	5 (12.8)	9 (16.7)	
Marital status													

Married	21 (80.8)	65 (89.0)	21 (80.8)	65 (87.8)	20 (83.3)	66 (86.8)	30 (83.3)	50 (87.7)	17 (85.0)	69 (86.3)	34 (87.2)	46 (85.2)	
Unmarried/divorced/widower	5 (19.2)	8 (10.8)	5 (14.7)	8 (13.6)	4 (16.7)	9 (11.8)	6 (16.7)	6 (10.5)	3 (15.0)	10 (12.5)	5 (12.8)	7 (13.0)	
Education													
High school or less	11 (42.3)	46 (62.2)	15 (44.1)	35 (59.3)	11 (45.8)	46 (60.5)	16 (44.4)	34 (59.6)	9 (45.0)	48 (60.0)	20 (51.3)	30 (55.6)	
Graduate	7 (26.9)	14 (18.9)	11 (32.4)	10 (17.0)	6 (25.0)	15 (19.7)	11 (30.6)	10 (17.5)	5 (25.0)	16 (20.0)	8 (20.5)	13 (24.1)	
Post-graduate	8 (30.8)	14 (18.9)	8 (23.5)	14 (23.7)	7 (29.2)	15 (19.7)	9 (25.0)	13 (22.8)	6 (30.0)	16 (20.0)	11 (28.2)	11 (20.4)	
Occupation													
Professional/Business	4 (15.4)	5 (6.7)	4 (11.8)	5 (8.5)	3 (12.5)	6 (7.9)	4 (11.1)	5 (8.8)	3 (15.0)	6 (7.5)	4 (10.3)	5 (9.3)	
Unskilled/field worker	5 (19.2)	9 (12.2)	6 (17.7)	8 (13.6)	4 (16.7)	10 (13.2)	6 (16.7)	8 (14.0)	5 (25.0)	9 (11.3)	4 (10.3)	10 (18.5)	
Housewife	16 (61.5)	58 (78.4)	22 (64.7)	45 (76.3)	16 (16.7)	58 (76.3)	24 (66.7)	43 (75.4)	12 (60.0)	62 (77.5)	29 (74.3)	38 (70.4)	
Retired/unemployed/student	1 (3.9)	2 (2.7)	2 (5.9)	1 (1.7)	1 (4.2)	2 (2.6)	2 (5.6)	1 (1.8)	0 (0.0)	3 (3.8)	2 (4.8)	1 (2.0)	
Residential location													
Rural	7 (26.9)	30 (40.5)	5 (14.7)	9 (26.5)	8 (33.3)	29 (38.2)	12 (33.3)	21 (38.2)	5 (25.0)	32 (40.0)	14 (35.9)	19 (35.2)	
Urban	19 (73.1)	42 (56.8)	25 (73.5)	25 (73.5)	16 (66.7)	45 (59.2)	24 (66.7)	34 (61.8)	15 (75.0)	46 (57.5)	24 (61.5)	34 (63.0)	
Cancer specific characteristics													
Cancer type													
Breast	12 (46.2)	48 (64.9)	14 (41.2)	41 (64.5)	11 (45.8)	49 (64.5)	14 (38.9)	41 (71.9)	8 (40.0)	52 (65.0)	19 (48.7)	36 (66.7)	
Ovary	10 (38.5)	16 (21.6)	7 (20.6)	17 (1.7)	7 (29.2)	19 (25.0)	9 (25.0)	15 (26.3)	6 (30.0)	20 (25.0)	8 (20.5)	16 (29.6)	
Others	4 (15.4)	10 (13.5)	13 (38.2)	17 (28.8)	6 (25.0)	8 (10.5)	13 (36.1)	1 (1.8)	6 (30.0)	8 (10.0)	12 (30.8)	2 (3.7)	
Illness duration													
Upto 1 year	8 (30.8)	18 (24.3)	9 (26.5)	15 (25.5)	11 (45.8)	15 (19.7)	11 (30.6)	13 (22.8)	6 (30.0)	20 (25.0)	11 (28.2)	13 (24.1)	
More than 1 year	18 (69.2)	56 (75.7)	25 (73.5)	44 (74.6)	13 (54.2)	61 (80.3)	25 (69.4)	44 (77.2)	14 (70.0)	60 (75.0)	28 (71.8)	41 (75.9)	
Treatment duration													
Upto 1 year	8 (30.8)	18 (24.3)	9 (26.5)	15 (25.4)	11 (45.8)	15 (19.7)	11 (30.6)	13 (22.8)	6 (30.0)	20 (25.0)	11 (28.2)	13 (24.1)	

More than 1 year	18 (69.2)	56 (75.7)	25 (73.5)	44 (75.6)	13 (54.2)	61 (80.3)	25 (69.4)	44 (77.2)	14 (70.0)	60 (75.0)	28 (71.8)	41 (75.9)	
Clinical approach													
0	1 (3.9)	4 (5.4)	5 (14.7)	0 (0.0)	2 (8.3)	3 (4.0)	5 (13.9)	0 (0.0)	2 (10.0)	3 (3.8)	5 (12.8)	0 (0.0)	
1	25 (96.2)	67 (90.5)	29 (85.3)	56 (94.9)	22 (91.7)	70 (92.1)	31 (86.1)	54 (94.7)	18 (90.0)	74 (92.5)	33 (84.6)	52 (96.3)	
Total	26	74	34	59	24	76	36	57	20	80	39	54	
Missing values are not shown													

Table-2: Frequencies and proportions of first degree relatives across demographic and cancer-related characteristics by the psychological outcomes of interest (n=52)

	Psychological outcomes of interest N (column %)											
	Pre-test anxiety		Post-test anxiety		Pre-test depression		Post-test depression		Pre-test DT		Post-test DT	
Characteristics	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Gender												
Female	4 (26.7)	16 (43.2)	10 (41.7)	10 (35.7)	6 (31.6)	14 (42.2)	9 (36.0)	11 (40.7)	7 (25.0)	13 (54.2)	15 (37.5)	5 (41.7)
Male	11 (73.3)	21 (56.8)	14 (58.3)	18 (64.3)	13 (68.4)	19 (57.6)	16 (64.0)	16 (59.3)	21 (75.0)	11 (45.8)	25 (62.5)	7 (58.3)
Religion												
Hindu	11 (73.3)	29 (78.4)	18 (75.0)	22 (78.6)	14 (73.4)	26 (78.8)	20 (80.0)	20 (74.1)	21 (75.0)	19 (79.2)	31 (77.5)	9 (75.0)
Others	4 (26.7)	8 (21.6)	6 (25.0)	6 (21.4)	5 (26.3)	7 (21.2)	5 (20.0)	7 (25.9)	7 (25.0)	5 (20.8)	9 (22.5)	3 (25.0)
Marital status												
Married	7 (46.7)	19 (51.4)	16 (66.7)	10 (35.7)	8 (42.1)	18 (54.6)	11 (44.0)	15 (55.6)	13 (46.4)	13 (54.2)	20 (50.0)	6 (50.0)
Unmarried/divorced	8 (53.3)	18 (48.7)	8 (33.3)	18 (64.3)	11 (57.9)	15 (45.5)	14 (56.0)	12 (44.4)	15 (53.6)	11 (45.8)	20 (50.0)	6 (50.0)
Education												
High school or lower	2 (13.3)	7 (18.9)	4 (16.7)	5 (17.9)	4 (21.1)	5 (15.2)	3 (12.0)	6 (22.2)	2 (7.1)	7 (29.2)	4 (10.0)	5 (41.7)
Graduate	8 (53.3)	22 (59.5)	14 (58.3)	16 (57.1)	9 (47.4)	21 (63.6)	17 (68.0)	13 (48.2)	17 (60.7)	13 (54.2)	25 (62.5)	5 (41.7)
Post-graduate	5 (33.3)	8 (21.6)	6 (25.0)	7 (21.2)	5 (20.0)	8 (29.6)	9 (32.1)	4 (16.7)	11 (27.5)	2 (16.7)	11 (27.5)	2 (16.7)
Occupation												
Professional/Business	2 (13.3)	9 (24.3)	5 (20.8)	6 (21.4)	3 (15.8)	8 (24.2)	4 (16.0)	7 (25.9)	6 (21.4)	5 (20.8)	10 (25.0)	1 (8.3)
Unskilled/field worker	6 (40.0)	9 (24.3)	6 (25.0)	9 (32.1)	6 (31.6)	9 (27.3)	9 (36.0)	6 (22.2	10 (35.7)	5 (20.8)	10 (25.0)	5 (41.7)

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Housewife	1 (6.7)	7 (18.9)	4 (16.7)	4 (14.3)	3 (15.8)	5 (15.2)	3 (12.0)	5 (18.5)	2 (7.1)	2 (25.0)	5 (12.5)	3 (25.0)
Retired/unemployed/student	6 (40.0)	12 (32.4)	9 (37.5)	9 (32.1)	7 (36.8)	11 (33.3)	9 (36.0)	9 (33.3)	10 (35.7)	8 (3.3)	15 (37.5)	3 (25.0)
Residential location												
Rural	4 (26.7)	14 (37.8)	5 (20.8)	13 (46.4)	6 (31.6)	12 (36.4)	7 (28.0)	11 (40.7)	6 (21.4)	12 (50.0)	12 (30.0)	6 (50.0)
Urban	11 (73.3)	23 (62.3)	19 (79.2)	15 (53.6)	13 (68.4)	21 (63.6)	18 (72.0)	16 (59.3)	22 (78.6)	12 (50.0)	28 (70.0)	6 (50.0)
Cancer specific characteristics												
Cancer type												
Breast	7 (46.7)	14 (37.8)	14 (58.3)	7 (25.0)	11 (57.9)	10 (30.3)	13 (52.0)	8 (29.6)	14 (50.0)	7 (29.2)	17 (42.5)	4 (33.3)
Ovary	5 (33.3)	3 (8.1)	2 (8.3)	6 (21.4)	4 (21.1)	4 (12.1)	2 (8.0)	6 (22.2)	5 (17.9)	3 (12.5)	5 (12.5)	3 (25.0)
Others	3 (20.0)	20 (54.1)	8 (33.3)	15 (53.6)	4 (21.1)	19 (57.6)	10 (40.0)	13 (48.2)	9 (32.1)	14 (58.3)	18 (45.0)	5 (41.7)
Total	15	37	24	28	19	33	25	27	28	24	40	12
Missing values are not shown												

Table-3: Association between pre genetic counselling and post counselling scores, controlling for cancer type and age

Exposures	Anxiety		Depression		Distress	
	OR	95% CI	OR	95% CI	OR	95% CI
Patients						
Crude	0.95	0.62, 1.46	0.64	0.39, 1.07	0.37	0.21, 0.68
*Adjusted	0.95	0.62, 1.46	0.64	0.38, 1.07	0.37	0.20, 0.68
Relatives						
Crude	1.42	0.68, 3.00	1.00	0.47, 2.15	0.60	0.29, 1.24
*Adjusted	1.05	0.44, 2.50	1.00	0.45, 2.22	0.60	0.29, 1.24
Non-hereditary cancers were excluded from these analyses *Adjusted for cancer type and age						

Table-3 shows that among patients, as compared to pre-genetic counselling, post-genetic counselling, the odds of having anxiety, depression, and distress were lower. For example, there was a 5% lower odds of anxiety post counselling (95% CI: 0.62, 1.46). However, the estimates were only significant for distress where after counselling as opposed to before, there were 63% lower odds (CI: 0.20, 0.68) of the former. Next, among the first degree relatives, as compared to pre-counselling, post-counselling estimates for anxiety show that although insignificant, relatives had slightly greater odds of experiencing the former (OR: 1.05; CI: 0.44, 2.50). For the same, the odds of experiencing distress were lower (OR: 0.60; CI: 0.29, 1.24)

DISCUSSION

Genetic counselling is relatively new in India, with first graduate level training being introduced in 2003.However, there exist variabilities and limitations among institutions offering these services[14].GTC services remain fragmented to date therefore. This pilot research effort was concerned with establishing the first such center at the premier most medical institute in India. This effort also addressed psychological symptoms among patients with familial cancer and their first degree relatives. Overall, our results indicated that counselling was associated with a significant reduction in distress among patients. Among relatives also a reduction was observed, however, this was not significant.

A previous study conducted among Breast Cancer patients in North India found that the prevalence of anxiety and depression respectively were 37% and 28%[15]. On the other hand, mild or greater depressive symptoms have been reported among 55% of the women with ovarian cancer[16]. In this study, considering only those with breast or ovarian cancer, over 70% each who had anxiety or depression at baseline had breast cancer and over 20% had ovarian cancer.

A previous meta-analysis of controlled trials showed that in general, there was no effect of genetic counselling on hereditary cancer-related anxiety (long term pooled difference = 0.05 U; -0.21, 0.31) and worry (-0.14; -0.35, 0.06)[9]. Similar results were reported by another study that found that among women affected by breast cancer, those who received GTC as opposed to those that did not, had comparable psychological morbidity[17].

Another randomized controlled trial investigating the impact of breast cancer risk counselling on distress among those with familial history reported that controlling for education level, those who received counselling had significantly lower distress than those who did not.Anxiety and distress was assessed among 412 women at risk of and those that had a previous history of familial cancer in a previous research effort[18-20]. While no significant change in anxiety levels were observed, worry about breast cancer reduced after a short term follow up and also at 6 months follow up. Also, no changes in worry about ovarian cancer were observed in general.

Our results showed that among patients, GTC had a significant protective effect against the psychological issues; however, this was just only significant for distress. Among relatives also post-counselling, although insignificant, there was a 40% reduction in the odds for distress. There was no association between counselling and anxiety or depression in our study, both among patients and their relatives.

LIMITATIONS

This was a pilot study and therefore had a small sample size. Another limitation was that the survey was self-administered which could have resulted in potential information bias. Collapsing the psychological outcomes categories into no and yes could have resulted in information loss as well. This study also lacked a control group and only did one group analysis.

CONCLUSIONS

This pilot research effort tried to fill the knowledge gap in GTC related research in Indian. Our results provide preliminary support to potential protective effect of GTC among cancer patients and their first-degree relatives for psychological distress related to the condition. While we did observe a protective effect of the former for depression as well among patients, this was not significant. A

future larger longitudinal study analyzing the association of interest is recommended. Future studies should also explore the role of treatment- and gender specific genetic counselling.

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