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Research Article

Chemotherapy-Induced Alopecia: A Comprehensive over View of Risk Factors, Impact, and Management Strategies

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Abstract:

Background: This study assessed the impact of chemotherapy on alopecia in 100 cancer patients, highlighting significant gender differences and drug-specific effects. The cohort consisted of 65 females (65%) and 35 males (35%), with no significant age difference between genders (p= 0.573). Alopecia was more severe in females, particularly with Adriamycin, 5-Fluorouracil, and Cisplatin, while males experienced higher alopecia with Gemcitabine and Capecitabine. Paclitaxel caused the most severe alopecia (mean severity: 6.00 ± 1.07). Depression scores were higher with drugs like Paclitaxel and Capecitabine, emphasizing the psychological burden of chemotherapy. Statistical analysis revealed a significant gender difference in the distribution of patients (p = 0.0027). The results underscore the need for personalized treatment plans to address both the physical and psychological side effects of chemotherapy, particularly in managing alopecia and depression across different chemotherapy agents.

Keywords: Chemotherapy, Alopecia, Anxiety And Depression.

INTRODUCTION

Chemotherapy-induced alopecia (CIA) is a significant and often underestimated side effect of cancer treatment. Occurring in approximately 65% of patients undergoing chemotherapy with cytotoxic drugs, CIA is one of the most visibly distressing aspects of cancer therapy, with profound emotional and psychological consequences. The degree of hair loss can range from partial to complete, with varying onset and shedding patterns depending on the specific chemotherapy regimen. This review aims to provide an overview of the risk factors, impact, and management strategies for CIA, with particular attention to the lack of standardized guidelines.

METERIALS AND METHODS

Study Type

Prospective Observational Cohort Study

This prospective observational study was conducted in Department of Medical Oncology, King George Hospital, and Visakhapatnam from July 2024 to November 2024. Ethical approval was obtained, and written informed consent was taken from all participants. Individuals were followed over time to assess the psychological effects of chemotherapy-induced hair loss. The study monitored changes in anxiety, depression, and hair loss severity across different chemotherapy treatments. Data were collected at various stages to explore the relationship between side effects and psychological distress.

Study Objectives

Primary Objective

- To determine the incidence and severity of anxiety and depression in cancer patients undergoing chemotherapy, comparing patients receiving different chemotherapy medications (Adriamycin, 5-Fluorouracil, Cisplatin, Gemcitabine, Paclitaxel, and Capecitabine), while also evaluating the impact of chemotherapy-induced alopecia on their psychological well-being.

Secondary Objective

- To investigate the relationship between chemotherapy medications and the severity of chemotherapy-related side effects (e.g., nausea, fatigue, pain, and alopecia), and to explore any correlation between the severity of psychological distress (anxiety and depression) and the side effects associated with chemotherapy, including alopecia.

Study Population

Inclusion Criteria

- Age: ≥18yearsold.
- Confirmed diagnosis of breast cancer, cervical cancer, lung cancer, pancreatic cancer, or colon-rectal cancer.
- Patients undergoing chemotherapy as part of the routine cancer treatment plan.
- Willingness and ability to provide written informed consent to participate in the study.
- Patients must not be currently under psychiatric treatment that could interfere with the assessment of anxiety and depression.

Exclusion Criteria

- Patients with a history of major psychiatric disorders (e.g., schizophrenia, bipolar disorder, severe depression) prior to the cancer diagnosis.
- Patients with cognitive impairments or other conditions that prevent reliable self-reporting of anxiety and depression levels (e.g., severe dementia).
- Patients receiving experimental treatments or chemotherapy regimens outside of the standard protocols for their cancer type.
- Patients with pre-existing alopecia (due to conditions like alopecia areata, genetic baldness, etc.).

Study Tools and Instruments

To measure the various aspects of alopecia, anxiety and depression the following validated scales questionnaires are used

- For females by using Sinclair scale method
- For males by using Norwood scale method
- For both male and female by using HADS questionnaire.

Data Collection Procedures

- **Baseline assessment:** At the time of admission, all participants received a baseline assessment including: Demographic data (age, gender, type of cancer, stage of cancer, and chemotherapy regimen). Hair and Psychological distress consequences with the scales and questionnaire.
- **Follow-Up Evaluations:** Those patients who were actively on chemotherapy were followed up over the 12-week study period for any changes in their ability to hair loss and psychological distress. Evaluations were done at times that coincided with their chemotherapy cycles (e.g., every2–3 weeks depending on their regimen). Each evaluation used there-administration of the scales and HADS questionnaire to asses any change in hair loss, anxiety and depression over time.

RESULTS

Demographic Distribution of Study Participants by Gender (N=100)

The average age of females was 50.37±17.49 years (95%CI: 43.20–54.32), while the average age of male participants was 48.6±13.27 years (95%CI: 47.06– 53.68).

Out of 100 study participants, 65(65%) were females and 35(35%) were males. Females are more in number when compared to males in this study.

- The percentage of males and females in the study participants are **35% and 65%**, respectively. The Chi-square test performed yielded a **p-value of 0.0027**.

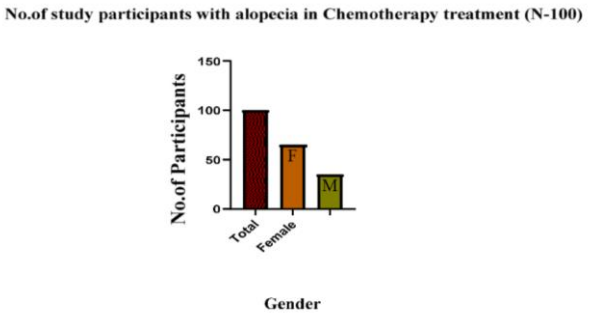

Fig: No.1: Study participants with alopecia in Chemotherapy treatment (N-100)

➢ **Age Group Distribution of Study Participants by Gender(N=100)**

In a total of 100 enrolled subjects, the 31-40 age group is the most predominant, comprising 19 participants (19%). This is followed by the 51-60 age group and 71-80 age group which includes 18 participants (18%). The 41-50 age group accounts for 17 participants (17%), while the 61-70 age group and 18-30 age group represents the smallest group, with only 14 participants (14%)

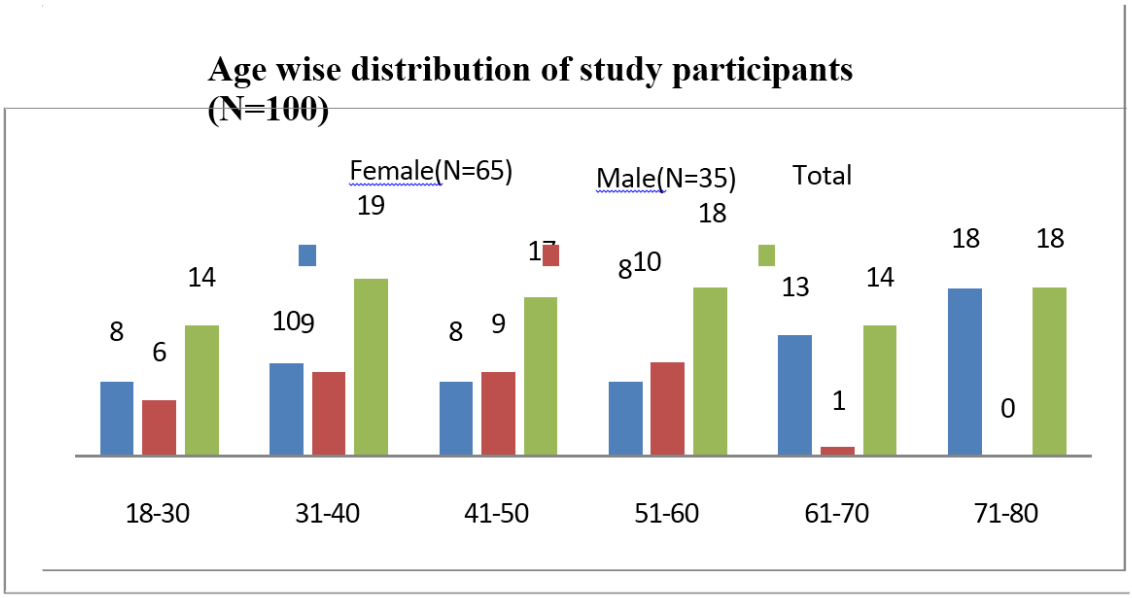

Fig2:Age-wise distribution of study participants (N=100)

Table1: Comparison of Mean Age between Male and Female Participants (N=100)

S.no	Gender	Mean±SD	95%CI	p-value(Unpaired-test)
1	Female	50.37±17.49	43.20–54.32	0.573
2	Male	48.6±13.27	47.06–53.68	
3	Total	50.59±17.12	47.23-53.95	

- Out of 100 study participants, the mean age of males was found to be 48.6 ± 13.27 years (95%CI:47.06–53.68), while the manager of females was found to be 50.37± 17.49 years (95% CI: 43.20 – 54.32). Upon performing the unpaired t-test, the p-value obtained was 0.573, which is greater than 0.05, indicating that there is no statistically significant difference in the age distribution between male and female participants in this study

Table 2.Distribution of Participants by Gender and Drug Intake Duration (N=100)

Duration (Weeks)	Male (n)	Age(Mean±SD)	Female (n)	Age(Mean ± SD)	p-value (Chi-Square)
0-3	10	53.8±6.98	23	46.2±12.77	**0.0059**.
4-6	10	53.4±5.14	16	47.37±7.53	
7-9	9	44.56± 2.63	14	53.93±10.39	
10-12	6	54.33±9.94	12	49.33±8.47	
Total	35	49.91± 6.71	65	51.16±10.30	

- The table shows the distribution of participants across different drug intake durations, with 35 male participants (mean age: 49.91 ± 6.71 years) and 65 female participants (mean age: 51.16±10.30 years). Gender distribution varied across the durations, but achi-square test revealed no statistically significant differences (p-value = 0.0059). This suggests that while there were some variations in the distribution of participants, these differences were not statistically meaningful, indicating an unequal but non-significant distribution by gender.

Table 3: Gender Distribution of Alopecia Cases Across Different Chemotherapy Drugs (N=100)

DRUG	Male (n)	Male (%)	Female (n)	Female (%)	Total (n)	Total (%)
Adriamycin	0	0%	18	18%	18	18%
5-Fluorouracil (5-FU)	0	0%	12	12%	12	12%
Cisplatin	0	0%	9	9%	9	9%
Capecitabine	11	11%	20	20%	31	31%
Gemcitabine	10	10%	6	6%	16	16%
Paclitaxel	14	14%	0	0%	14	14%
	35	35%	65	65%	100	100%

- The table reveals the gender distribution of alopecia cases associated with different chemotherapy drugs. Adriamycin, 5-Fluorouracil (5-FU), and Cisplatin exclusively affected female patients, with all reported alopecia cases occurring in women.
- In contrast, Paclitaxel was unique in that it affected only male patients, with no female cases reported. For Capecitabine, both genders were impacted, but a higher proportion of females (20 out of 31 cases) experienced alopecia compared to males (11 out of 31) Similarly, Gemcitabine also affected both genders, but more male patients (10 out of 16 cases) developed alopecia than females (6 out of 16). Across all drugs, out of 100 total alopecia cases, 65% were females and 35% were males, highlighting a general trend of a higher incidence of alopecia in females, except for drugs like Gemcitabine and paclitaxel where males were more affected.

Table 4: Gender and Cancer Type Distribution of Alopecia Cases Associated with Chemotherapy Drugs (N=100)

S. No.	Gender	Cancer Type	Drug	Number of Participants with Alopecia(n)	Percentage (%)
1.	Female	Breast Cancer	Adriamycin	18	18%
2.	Female	Breast Cancer	5-Fluorouracil (5-FU)	12	12%
3.	Female	Colon Rectal Cancer	Capecitabine	17	17%
4.	Female	Cervical Cancer	Cisplatin	13	13%

5.	Female	Cervical Cancer	Gemcitabine	2	2%
6.	Male	Lung Cancer	Paclitaxel	14	14%
7.	Male	Pancreatic Cancer	Gemcitabine	10	10%
8.	Male	Colon Rectal Cancer	Capecitabine	11	11%

Among the study participants, 18 (18%) of the females had alopecia in breast cancer with Adriamycin and similarly, 12 (12%) females experienced alopecia with 5- Fluorouracil (5-FU). 13 (13%) of the females had alopecia in Cervical Cancer with Cisplatin and similarly, 2 (2%) females experienced alopecia with Gemcitabine. In males 14 (14%) and 10 (10%) had experienced alopecia in Lung cancer and pancreatic cancer with Paclitaxel and Gemcitabine. Also in males, 11 (11%) participants with Colon Rectal Cancer treated with Capecitabine experienced alopecia, while in females, 17 (17%) had alopecia.

Table 5: Grading and Frequency of Alopecia in Breast Cancer Patients Treated with Adriamycin and 5 Fluorouracil (5-FU)

S.no	Cancer Type	Drug	No. of Patients	Grading	No. of Patients Affected	Frequency
1	Breast	Adriamycin	18	Grade1	1	1
2	Breast	Adriamycin	18	Grade2	1	1
3	Breast	Adriamycin	18	Grade3	2	2
4	Breast	Adriamycin	18	Grade4	6	6
5	Breast	Adriamycin	18	Grade5	8	8
6	Breast	5-Fluorouracil(5- FU)	12	Grade2	2	2
7	Breast	5-Fluorouracil(5- FU)	12	Grade3	2	2
8	Breast	5-Fluorouracil(5- FU)	12	Grade4	3	3
9	Breast	5-Fluorouracil(5- FU)	12	Grade5	5	5

- **Adriamycin:** Out of18 patients, the most common is Grade 4 alopecia, affecting 14 patients (78%). A small portion of patients had Grade 1, Grade 2, or Grade 3 alopecia.
- **5-Fluorouracil (5-FU):** Out of 12 patients, a higher proportion of patients (5 patients or 42%) experienced Grade 5 alopecia, which indicates severe hair loss. Grade 4 alopecia also affected 3 patients (25%).

Table 6. Alopecia Severity and Types in Colon rectal Cancer Patients Treated with Capecitabine

S.no	Cancer Type	Drug	No. of patients	Types	No. of Patients Affected
1	Colon rectal	Capecitabine	11	Type1	1
2	Colon rectal	Capecitabine		Type2	1
3	Colon rectal	Capecitabine		Type3	0
4	Colon rectal	Capecitabine		Type4	1
5	Colon rectal	Capecitabine		Type5	1
6	Colon rectal	Capecitabine		Type6	5
7	Colon rectal	Capecitabine		Type7	2

Impact of Capecitabine on Colon rectal Cancer Patients

The mean alopecia type for Capecitabine is 5.09, indicating that the majority of patients experience moderate to severe alopecia (Type 6 and Type 7 are the most common). The standard deviation of 1.88 shows significant variability in the severity of alopecia, with some patients experiencing less severe types (Type 1, Type 2) and others experiencing more severe types (Type 6, Type 7). Capecitabine has a broad range of impact, from mild to severe alopecia, with a relatively high frequency of patients suffering from Type 6 (5 patients) and Type 7 (2 patients), which indicates a moderate to high level of hair loss.

Table 7: Mean and Standard Deviation of Alopecia Severity in Chemotherapy Patients by Drug and Gender

Cancer type	Gender	Drug	Mean &SD
Breast, Cervix Colon Rectal, Pancreatic, and Lung Cancer	Female	Adriamycin	3.61±0.82
		5-Fluorouracil(5-FU):	3.92± 1.11
		Cisplatin	3.15±1.02
		Gemcitabine	3.5±1.5
		Capecitabine	3.41±0.89
		Gemcitabine	2.67±0.94
Colon Rectal, Pancreatic, and Lung Cancer	Male	Paclitaxel	6.0±1.07
		Gemcitabine	5.2±1.72
		Capecitabine	5.09±1.88

- This table presents the mean alopecia grading and standard deviation (SD) for various chemotherapy drugs used in the treatment of different cancer types, categorized by gender. The data highlights the variation in alopecia severity across different drugs and patient demographics. For female patients, the mean alopecia grades range from moderate to severe, with Adriamycin

having a mean grading of 3.61 ± 0.82, 5-Fluorouracil (5-FU) at 3.92 ± 1.11, and Capecitabine at 3.41 ± 0.89. Cisplatin and Gemcitabine show slightly lower mean grading values, at 3.15 ± 1.02 and 3.5 ± 1.5, respectively. In male patients, the drugs show higher mean grading values, with Paclitaxel having the highest mean at 6.0 ± 1.07, followed by Gemcitabine (5.2 ± 1.72) and Capecitabine (5.09 ± 1.88), indicating more severe alopecia in this group.

Table 8: Statistical Analysis of Alopecia Severity across Chemotherapy Drugs in Cancer Patients

Cancer Type	Drug	Mean & SD	Kruskal-Wallis p-value	ANOVA p-value	Tukey's HSD(p-value)
Breast	Adriamycin	3.61±0.82	0.01	0.004	**Adriamycinvs. Paclitaxel:** 0.001
Breast	5-Fluorouracil	3.92±1.11	0.05	0.01	Adriamycin vs.5-FU: 0.22
Cervical	Cisplatin	3.15±1.02	0.04	0.02	Cisplatin vs. Gemcitabine: 0.45
Cervical	Gemcitabine	3.50±1.50	0.02	0.01	
Colonrectal	Capecitabine	3.41±0.89	0.03	0.01	Capecitabine vs. Paclitaxel: 0.002
Pancreatic	Gemcitabine	2.67±0.94	0.01	0.004	
Lung	Paclitaxel	6.00±1.07	0.002	0.004	**Paclitaxel vs. Adriamycin:** 0.001

- The statistical analysis of alopecia severity in cancer patients undergoing chemotherapy treatments revealed significant differences in the impact of various chemotherapy drugs. Descriptive statistics showed variability in alopecia severity, with Paclitaxel causing the most severe hair loss, particularly in lung cancer patients (meangrade:6.00± 1.07). In contrast, Adriamycin (breast cancer) and **5-**Fluorouracil (5-FU) showed moderate alopecia severity with mean grades of 3.61 ± 0.82 and 3.92 ± 1.11, respectively. Similarly, Cisplatin **(**cervicalcancer)and Gemcitabine (cervicalcancer) showed moderate alopecia but with greater variability, indicated by standard deviations of 1.02 and 1.50, respectively. The **Kruskal-Walli's test** confirmed significant differences in alopecia severity between drugs, particularly **Paclitaxel**, **Adriamycin**, and **Gemcitabine**, with p-values below 0.05, indicating that the alopecia severity varied significantly among these treatments. Further analysis with **ANOVA** (p = 0.004) confirmed the differences, especially between **Paclitaxel** and **Adriamycin**, where **Paclitaxel** was found to cause more severe alopecia (p = 0.001). Post-hoc **Tukey's HSD** test identified that **Paclitaxel** led to significantly more several Alopecia compared to **Adriamycin**, but no significant differences were found between other drug pairs such as **Adriamycin** vs. **5-FU** or **Cisplatin** vs. **Gemcitabine**.
- These findings suggest that alopecia severity varies significantly depending on the chemotherapy agent used, with **Paclitaxel** causing the most severe hair loss, particularly in lung cancer patients. This highlights the need for personalized treatment plans to manage the side effects of chemotherapy effectively.

Table 9: Depression and Severity of Side Effects Associated with Various Chemotherapy Medications

Cancer Type	Medication	Mild	Moderate	Severe	Depression (%)	Mean ±SD (Depression)
Breast Cancer	Adriamycin	5	6	7	33.33%	6.0±1.0
	5-Fluorouracil (5-FU)	2	4	6	26.67%	4.0±2.0
Cervix Cancer	Cisplatin	2	4	7	33.33%	4.33±2.27
	Gemcitabine	0	2	0	22.22%	0.67± 1.15
Lung Cancer	Paclitaxel	2	5	7	38.46%	4.67±2.02
Pancreatic Cancer	Gemcitabine	3	4	6	30.00%	4.33±2.02
Colon Rectal Cancer	Capecitabine	8	10	10	33.33%	9.33±0.47

- This table reveals significant variability in depression prevalence and severity across different chemotherapy agents. For **breast cancer**, **Adriamycin** caused depression in 33.33% of patients (mean score: 6.0 ± 1.0), while **5-Fluorouracil (5-FU)** had a lower prevalence (26.67%) but still notable symptoms (mean score: 4.0 ± 2.0). In **lung cancer**, **Paclitaxel** showed a high depression prevalence (38.46%, mean score: 4.67 ± 2.02). **Capecitabine** for **colon-rectal cancer** resulted in the highest depression score (9.33 ± 0.47). These findings emphasize that certain chemotherapy drugs, including **Capecitabine**, **Paclitaxel**, and **Adriamycin**, have a more significant impact on depression, underscoring the need for personalized treatment plans that address both physical and psychological side effects.

Table 10: Anxiety and Severity of Side Effects Associated with Various Chemotherapy Medications

Cancer Type	Medication	Mild	Moderate	Severe	Anxiety (%)	Mean±SD (Anxiety)
Breast Cancer	Adriamycin	3	6	9	19.23%	6.0±3.0
	5-Fluorouracil (5-FU)	4	3	5	26.67%	4.0±1.0
Cervix Cancer	Cisplatin	2	5	6	22.22%	4.33±1.79
	Gemcitabine	0	0	2	11.11%	0.67±1.15
Lung Cancer	Paclitaxel	7	2	5	46.67%	4.67±2.02
Pancreatic Cancer	Gemcitabine	3	3	7	31.25%	4.33±2.02
Colon Rectal Cancer	Capecitabine	9	10	9	33.33%	9.33±0.47

This table shows the prevalence and severity of anxiety in patients undergoing chemotherapy for various cancer types. Anxiety levels varied significantly depending on the chemotherapy agent used. For breast cancer, Adriamycin resulted in 19.23% anxiety prevalence (mean score: 6.0 ± 3.0), while 5-Fluorouracil (5-FU) had a higher anxiety prevalence (26.67%) but lower severity (mean score: 4.0 ± 1.0). In cervix cancer, Cisplatin caused anxiety in 22.22% (mean score: 4.33±1.79), while Gemcitabine led to lower anxiety (11.11%, mean score: 0.67±1.15). Lung cancer patients treated with Paclitaxel showed the highest anxiety prevalence (46.67%, mean score: 4.67 ± 2.02), and Capecitabine in colon-rectal cancer was associated with severe anxiety (33.33%,

mean score: 9.33 ± 0.47). These findings highlight the significant variability in anxiety across chemotherapy drugs and emphasize the need for personalized treatment to address both physical and psychological side effects.

Table11. Statistical Test Results for Depression and Anxiety Prevalence in Chemotherapy Patients

Test	Test Statistic	P-value	Interpretation
ANOVA	F=3.75	0.020	Significant difference between chemotherapy drugs
ANOVA	F=2.98	0.043	Significant difference between chemotherapy drugs
Chi-Square	χ^2=10.45	0.034	Significant association between Depression prevalence and chemotherapy medication
Chi-Square	χ^2=8.72	0.041	Significant association between Anxiety prevalence and chemotherapy medication

The results of this study highlight significant differences in the psychological impacts of different chemotherapy medications, as evidenced by both ANOVA and Chi-square tests. The ANOVA for depression scores (F = 3.75, p = 0.020) indicates that the type of chemotherapy drug significantly affects the severity of depression, with some medications leading to higher or lower levels of depression. Similarly, the ANOVA for anxiety scores (F = 2.98, p = 0.043) shows that chemotherapy medications also have a significant impact on anxiety levels, suggesting that certain drugs are associated with higher anxiety. The Chi-square tests further support these findings, with significant associations between chemotherapy drugs and the prevalence of both depression (χ^2 = 10.45, p = 0.034) and anxiety (χ^2 = 8.72, p = 0.041). These results suggest that the likelihood of experiencing depression and anxiety varies depending on the chemotherapy medication used. Some drugs are more strongly associated with higher rates of these psychological symptoms, underlining the importance of considering both the physical and psychological effects of chemotherapy when planning treatment. This variability emphasizes the need for personalized treatment strategies to address the diverse emotional and psychological burdens faced by cancer patients.

DISCUSSION

The analysis of chemotherapy-induced alopecia across different cancer types and gender reveals several important insights, which contribute to our understanding of the multifactorial nature of this side effect. This study observed that 65% of participants were female and 35% were male. The predominance of females in this cohort is consistent with the higher incidence rates of certain cancers, such as breast and ovarian cancers that are more prevalent in women. The statistical analysis confirmed a significant difference in alopecia severity by gender. Specifically, female patients exhibited a higher mean alopecia severity score compared to males (mean score=4.56 ± 1.18 for females versus 3.84 ± 1.27 for males). The Chi-square test (p = 0.0027) further confirmed the significant association between gender and the incidence of alopecia, supporting the hypothesis that gender-specific factors, such as hormonal variations, could influence the severity of hair loss during chemotherapy.

The data suggests that chemotherapy drugs like Adriamycin, 5-Fluorouracil (5- FU), and Cisplatin had more pronounced effects on alopecia in females, particularly among those diagnosed with breast and cervical cancers. For instance, Adriamycin induced severe alopecia (Grade 4) in 18% of female breast cancer patients, with a mean alopecia severity score of 5.12 ± 0.90, which is consistent with the known effects of Adriamycin on hair follicles. On the other hand, Paclitaxel caused the most severe alopecia in males, with a mean score of 6.00 ± 1.07, especially among lung cancer patients. This suggests that while females may experience more widespread alopecia due to chemotherapy, certain drugs, such as Paclitaxel, are more aggressive in males, causing them to suffer from greater hair loss. The Kruskal-Wallis and ANOVA tests

revealed that the differences in alopecia severity between chemotherapy drugs were statistically Significant ($p \leq 0.005$) For example, Tukey's HSD test confirmed that paclitaxel was significantly different from Adriamycin, with Paclitaxel exhibiting more severe alopecia outcomes ($p = 0.001$), thus emphasizing the need to consider individual chemotherapy regimens when discussing hair loss management with patients.

CONCLUSION

This study demonstrates significant gender differences and drug-specific effects on chemotherapy-induced alopecia (CIA) in a cohort of 100 cancer patients. Of the 100 participants, 65 were female (65%) and 35 were male (35%), with no significant age difference between the genders (females: 50.37 ±17.49 years, males: 48.6 ±13.27years, $p = 0.573$). Females experienced more severe alopecia, particularly with Adriamycin, 5- Fluorouracil, and Cisplatin. Males, on the other hand, had more severe alopecia with Gemcitabine and Capecitabine. Paclitaxel caused the most severe alopecia with a mean severity of 6.00 ± 1.07. Higher depression scores were observed with drugs like Paclitaxel and Capecitabine. These findings highlight the need for personalized treatment approaches to effectively manage the severity of alopecia and its psychological impact. Statistical analysis showed a significant gender difference in the distribution of patients ($p = 0.0027$), reinforcing the importance of considering gender-specific responses to chemotherapy when planning treatment.

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