# FACTORS ASSOCIATED WITH COMPLIANCE TO CHEMOTHERAPY AMONGST CANCER PATIENTS IN A RADIOTHERAPY FACILITY

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## ABSTRACT

**Objectives:** To study compliance with chemotherapy schedules in cancer patients and associated factors.
**Study Background:** This study was conducted in Radiotherapy/Oncology Department, Ahmadu Bello University Teaching Hospital (ABUTH) Zaria which has a 10-bed capacity chemotherapy room, within 11 weeks from 1st March 2018 to 18th May 2018. Almost all the patients were on 3- weekly cyclical chemotherapy with very few patients on 2-weekly or 4- weekly courses. The hospital serves as a centre of excellence for oncology in the Northern region of Nigeria. The bulk of the patients are from a low socio-economic class.
**Methodology:** The study is a prospective cross-sectional study involving a total of 140 patients. Data collection from patients' record (age, diagnosis, stage at diagnosis, comorbidities, chemotherapy regimen, previous treatments received etc.), the record of the date of chemotherapy course and assessment ECOG performance for each patient during each chemotherapy course were recorded in a designed booklet. This was conducted for over 11 weeks. Ethical clearance was obtained. Patients' consent was obtained, and care was taken to maintain the confidentiality of patients. Data collected were inputted and analyzed using Statistical Program for Social Sciences (SPSS) version 21.0.
**Results:** There was a statistically significant correlation between compliance with chemotherapy schedule and patients' performance status, prior radiotherapy, combination chemotherapy and use of platinum-based chemotherapy regimen. However, there were no correlations with patients' age, sex, chemotherapy course, stage of the disease, previous oncology-related surgery (excluding biopsies), comorbidities and blood transfusion during chemotherapy.
**Conclusion:** This study suggests that patients' performance status, prior radiotherapy, use of platinum-based chemotherapy and combination chemotherapy schedule are significant to compliance with chemotherapy.

# INTRODUCTION

Chemotherapy is the use of cytotoxic drugs and hormones in the treatment of cancer. It is a systemic therapy that kills cells of the primary tumour and malignant cells that may be circulating in the body.[1] Chemotherapy agents affect tumour cells as well as malignant cells, thereby causing therapeutic as well as toxic effects respectively. Using the knowledge of tumour kinetics, principles of combination chemotherapy and administration of premedication, the Oncologist aims to maximize the therapeutic benefits, while minimizing the adverse effects of chemotherapy[2].

Chemotherapy is used in combination with other modalities of treatment like surgery and radiotherapy to achieve cure in patients presenting with early-stage or palliation in locally advanced or metastatic cancers. When used before, or after these modalities, they are known as neoadjuvant and adjuvant chemotherapy, respectively[3].

Not many works of literature are available on compliance with chemotherapy. However, a study found weekly compliance of 62% and monthly compliance of 83% in cancer patients (n= 286) which was significantly associated with older age, higher education and initial 12 weeks of treatment[4]. A similar study on osteosarcoma patients on chemotherapy (n= 124) found compliance amongst patient to be 64% which was significantly associated with good response of tumours to chemotherapy. However, there was no difference in survival between compliant and non-compliant patients[5]. Poor compliance amongst breast and gynaecological cancer patients on chemotherapy was also found to be significantly associated with adverse effects on taste and smell[6]. In a comparative study between colorectal cancer patients with similar demographic characteristics who received their chemotherapy on outpatient basis or at home, it was found that there was a significant difference in non- compliance (14% outpatient vs 2% at home) which was attributed to more expression of satisfaction in the later group than the former. However, no difference in outcome in both patients[7]. Compliance was also found to be significantly associated with the use of educational materials amongst female breast cancer patients on aromatase inhibitor[8].

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In order to maximize the benefit of chemotherapy, compliance to prescribed courses as at when due is of utmost importance. This research aims to study the incidence of non- compliance with chemotherapy and factors associated with it.

## METHODOLOGY

The study is a cross-sectional study involving a total of 140 patients. The study population includes patients who received chemotherapy at Radiotherapy/Oncology Department, Ahmadu Bello University Teaching Hospital, Zaria within the period of study. The Eastern Cooperative Oncology Group (ECOG) performance status was used to access the patients' fitness during each chemotherapy course by the researchers and was recorded appropriately [9]. Patients were grouped into ECOG 0-1, and 2 in decreasing order of fitness. Patients having an ECOG score of 3 or 4 were not given chemotherapy. The dates of each chemotherapy course of the patients were recorded, and only patients who had received at least 4 courses of chemotherapy were included in the study. For this study, compliance is receipt of planned cycles of chemotherapy in the scheduled doses within the planned duration of up to 25% additional time [5].

Data collection from patients' record (age, diagnosis, stage at diagnosis, comorbidities, chemotherapy regimen, previous treatments received etc.), the record of the date of chemotherapy course and assessment ECOG performance for each patient during each chemotherapy course were recorded in a designed booklet made for the purpose of this research. Patients' subsequent information was recorded as a continuation of the previous ones and care was taken to avoid missing or duplication of data.

Ethical approval was obtained from Health Research, and Ethical Committee ABUTH, strict confidentiality was maintained, and informed consent of the patient was sought.

The study was conducted over a period of 11 weeks (1st March to 18th May 2018). Data obtained were inputted and analyzed using Statistical Program for Social Sciences (SPSS) version 21.0 were an association between various demographic and clinical parameters were tested for significance with compliance using Pearson Chi-squaree. A confidence interval of 5% was used for the purpose of this research.

## EXCLUSION CRITERIA

Patients, who commenced their first course of chemotherapy towards the end of the period of study, such that their scheduled second course was outside the period of study, were excluded

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this study.

## RESULTS

The demographic information of the patients is presented in Table 1 below. The mean age of the patients was 48.5 years, with a standard deviation of 15.8 years and a range of 9 years – 85 years. However, the mean and standard deviation for the female cancer patients was slightly lower than those of the males (Table 1). Majorityofthe patients were females (60%), with the Male to Female ratio of 1.0: 1.5. Almost half of the total number of patients (47.9%) fell within the age group of 40 years – 59 years (Table 1).

Cervical cancer (35.7%) and breast cancer (29.8%) were the commonest female malignancies while Head and Neck tumours (26.8%) were the most prevalent group of tumours amongst the male groups (Table 1)

**Table 1. Demographic and Cancer distribution of patients on chemotherapy**

| Variable | Male (years) | Female (years) | Total (years) |
|---|---|---|---|
| Mean | 49.4 | 47.9 | 48.5 |
| Standard Deviation | 17.3 | 14.8 | 15.8 |
| Range | 9 - 85 | 16 – 85 | 9- 85 |
| | | | |
| Variable | Male (%/ freq) | Female (%/freq) | Total (%/freq) |
| Cancer patients | 40.0 (56) | 60.0 (84) | 100 (140) |
| | | | |
| Age Distribution | | | |
| Young (0- 39 years) | 12.2 (17) | 15.7 (22) | 27.9 (39) |
| Middle (40- 59 years) | 16.4 (23) | 31.5 (44) | 47.9 (67) |
| Elderly ( 60 years) | 11.4 (16) | 12.8 (18) | 24.2 (34) |
| | | | |
| Compliant | 42.9 (24) | 53.6 (45) | 49.3 (69) |
| Non- complaint | 57.1 (32) | 46.4 (39) | 51.7 (71) |
| | | | |
| Cancers Distribution | | | |
| Cervix | --- | 35.7 (30) | 21.4 (30) |
| Breast | --- | 29.8 (25) | 17.9 (25) |
| Head and Neck | 26.8 (15) | 6.0 (5) | 14.3 (20) |
| Colorectal | 8.9 (5) | 6.0 (5) | 7.9 (11) |
| Soft Tissue Sarcoma | 7.1 (4) | 4.8 (4) | 5.7 (8) |
| Prostate | 10.7 (6) | --- | 4.3 (6) |
| Ovary | --- | 7.1 (6) | 4.3 (6) |
| Urinary Bladder | 10.7 (6) | 1.2 (1) | 5.0 (7) |
| SCC of Skin | 7.1 (4) | 2.4 (2) | 4.3 (6) |
| Others | 29.6 (16) | 7.1 (6) | 15.7 (22) |
| | | | |
| TOTAL | 40.0 (56) | 60.0 (84) | 100 (140) |

Table 2. Association between compliance to chemotherapy schedule and variable factors

| Variables | Compliant (%/freq) | Non-complaint (%/freq) | Total (freq) | Significance (Pearson Chi Square) |
|---|---|---|---|---|
| **Age** | | | | |
| Young (0- 39 yrs) | 51.3 (20) | 48.7 (19) | 39 | 0.570 |
| Middle (40- 59yrs) | 49.3 (33) | 50.7 (34) | 67 | |
| Elderly (60 yrs +) | 47.1 (16) | 52.9 (18) | 34 | |
| | | | | |
| **Sex** | | | | |
| Male | 42.9 (24) | 57.1 (32) | 56 | 0.214 |
| Female | 53.6 (45) | 46.4 (31) | 84 | |
| | | | | |
| **Stage of Disease** | | | | |
| Early | 61.5 (8) | 38.5 (5) | 13 | 0.571 |
| Locally advanced | 49.5 (45) | 50.5 (46) | 91 | |
| Metastatic | 44.4 (16) | 55.6 (20) | 36 | |
| | | | | |
| **ECOG Score** | | | | |
| 0-1 all through | 54.3 (51) | 45.7 (43) | 94 | 0.001 |
| 2, but improved | 73.3 (11) | 26.7 (4) | 15 | |
| 2, didn't improve | 20.7 (6) | 79.3 (23) | 29 | |
| | | | | |
| **Co morbidities** | | | | |
| Present | 59.3 (16) | 40.7 (11) | 27 | 0.249 |
| Absent | 46.9 (53) | 53.1 (60) | 113 | |
| | | | | |
| **Chemotherapy Course** | | | | |
| First | 53.6 (60) | 46.4 (52) | 112 | 0.128 |
| Second or Third | 32.1 (9) | 67.1 (19) | 28 | |
| | | | | |
| **Surgery (cancer related, excluding biopsies)** | | | | |
| Had surgery | 45.6 (26) | 54.4 (31) | 57 | 0.471 |
| No surgery | 51.8 (43) | 48.2 (40) | 83 | |
| | | | | |
| **Radiotherapy** | | | | |
| Had Radiotherapy | 12.5 (1) | 87.5 (7) | 8 | 0.032 |
| No Radiotherapy | 51.5 (68) | 48.5 (64) | 132 | |
| | | | | |
| **TOTAL** | **49.3 (69)** | **50.7 (71)** | **100 (140)** | |

Table 3. Association between compliance to chemotherapy schedule and variable factors

| Variables | Compliant (%/freq) | Non-complaint (%/freq) | Total (freq) | Significance (Pearson Chi Square) |
|---|---|---|---|---|
| **Blood transfusion** | | | | |
| Had transfusion | 48.1 (39) | 51.9 (42) | 81 | 0.752 |
| No transfusion | 50.8 (30) | 49.2 (29) | 59 | |
| | | | | |
| **Number of Chemotherapy agents** | | | | |
| | | | | |
| Single agent | 22.7 (5) | 77.3 (17) | 22 | 0.007 |
| Combination | 53.8 (63) | 46.2 (54) | 117 | |
| | | | | |
| **Number of Days of Cycle** | | | | |
| | | | | |
| Single day | 47.8 (55) | 52.2 (60) | 115 | 0.459 |
| Multi- days | 56.0 (14) | 44.0 (11) | 25 | |
| | | | | |
| **Chemotherapy Regimen** | | | | |
| | | | | |
| Platinum based | 59.2 (45) | 51.0 (26) | 76 | 0.010 |
| Non- Platinum based | 37.5 (24) | 62.5 (40) | 64 | |
| | | | | |
| Paclitaxel based | 49.0 (25) | 51.0 (26) | 51 | 0.962 |
| Non Paclitaxel based | 49.4 (44) | 50.6 (45) | 89 | |
| | | | | |
| Cyclophosph. based | 48.4 (15) | 51.6 (16) | 31 | 0.910 |
| Non Cycloph. based | 49.4 (54) | 50.5 (55) | 109 | |
| | | | | |
| Adramycin based | 52.8 (19) | 47.2 (17) | 36 | 0.627 |
| Non Adriamycin based | 48.1 (50) | 51.9 (54) | 104 | |
| | | | | |
| 5- FU based | 54.5 (18) | 45.5 (15) | 33 | 0.459 |
| Non 5-FU based | 47.2 (50) | 52.8 (56) | 106 | |
| | | | | |
| **TOTAL** | **49.3 (69)** | **50.7 (71)** | **100 (140)** | |

**134**

## DISCUSSION

The Male to Female ratio in this study was 1.0: 1.5 This in agreement with many recent studies done on cancer in Nigeria which show a higher burden of cancer on female gender [10, 11, 12]. The higher incidence of cancer amongst females is due to the high incidence of cervical and breast cancers in the female population. This is in contrast to what is obtainable in the United States of America, where Male to Female ratio is 1.2: 1.0 where cancer incidence is higher amongst males despite breast cancer being the second commonest cancer [13]. This contrast could be explained by the fact that cervical cancer does not feature amongst the top 10 cancers affecting women in the United States [13] while its incidence is on the rise in Nigeria, and the second commonest female cancer [12], hence the disparity.

The study also showed that nearly half (49.3%) of the patients receiving chemotherapy were compliant to their chemotherapy schedule with better compliance amongst the female group (53.6%) compared to the males (42.9%). However, this was not statistically significant (p=, 0.570). This result is worse than a similar study mentioned, which recorded compliance of 83%, 64% and 86- 98% respectively [4, 5, 7], but better than a Nigerian breast study, where 80.9% of patients were not complaint [14]. The high incidence of non-compliance in this study is of importance as previous studies demonstrated its negative influence on the quality of life in patients and treatment outcomes [15]. The study, however, was not able to follow up patients, who ultimately defaulted without completing their chemotherapy to ascertain treatment outcomes or their reasons for defaulting.

The performance status of patients in the study was significantly correlated with compliance to chemotherapy (p= 0.001). Those with good performance status (ECOG 0-1), or improved in their performance status during subsequent cycles of chemotherapy had better compliance than those who didn't improve in performance status. This finding is consistent with studies done in this regard [5, 16]. It is worthy of note that patients in the study centre with very poor performance status (ECOG 3-4) neither commenced nor continued chemotherapy until they had improved (to at least ECOG 2) in accordance with ASCO recommendation [17].

Patients who had radiotherapy prior to chemotherapy course in this study were significantly non-compliant compared to those who had no radiotherapy (p=0.032). Even though the number of patients who had radiotherapy in this study was small (n= 8) due to non-functional radiotherapy machines in the centre for the period of study, a possible explanation of this result is that those who had radiotherapy have had cancer treatment for longer duration and probably 'fatigued', less enthusiastic or losing hope on treatment compared to those who are radiotherapy naïve.

The uses of combination chemotherapy (p= 0.007) and platinum-based (Cisplatin or Carboplatin) chemotherapy (p= 0.010) have been associated with compliance in patients in this study. This can be explained by the fact that the use of cisplatin-based chemotherapy is associated with improved treatment outcome [18, 19, 20, 21]. However, despite its impressive anti-tumour activity, treatment with cisplatin-based chemotherapy can result in severe toxicity [22] which

should result in less compliance as opposed to the result of this study. Hence, further research on this aspect is suggested. Single-agent chemotherapy is most often used in palliative settings and may account for its association with non- compliance amongst cancer patients.

There was no correlation between compliance and age, sex, stage of the disease, presence of comorbidities, chemotherapy course, previous cancer-related surgery, blood transfusion during chemotherapy cycle, number of days of cycle or chemotherapy regimen order than platinum-based. Even though a significant proportion (48.1%) of the cancer patients had a blood transfusion during their chemotherapy cycles, no correlation was derived with compliance.

## CONCLUSION

This study showed compliance of 49.3% in all cancer patients, which was significantly associated with patients' performance status, prior radiotherapy, use of platinum-based chemotherapy and combination chemotherapy.

## LIMITATIONS

The study could not objectively measure the socio-economic status of patients, cost of chemotherapy and logistics and distance and accessibility of residence of the patient to the hospital and adverse effects to chemotherapy experienced by patients.

## ACKNOWLEDGEMENT

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**135**

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**136**