Original Research Article

ASSESSMENT OF MEDICATION ADHERENCE TO ORAL ANTINEOPLASTIC DRUGS AMONG CANCER PATIENTS IN A TERTIARY HOSPITAL IN SOUTH-SOUTH, NIGERIA

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ABSTRACT

The prevalence of cancer in developing countries is on the increase, and is associated with a high mortality rate. The study aimed to evaluate medication adherence to oral antineoplastic therapy in a tertiary health facility, in Benin City.
A cross-sectional study was carried out among cancer patients at the oncology unit of the University of Benin Teaching Hospital, Benin City, using semi-structured and standardized Morisky Green Test instruments. The analysis was descriptive and inferential, and the results were considered significant at $p < 0.05$. Medication adherence to oral antineoplastic drugs was 74.4%. The patients had a significant ($p < 0.05$) Morisky Green Test score of 25.6%. Respondents using Bevacizumab, Docetaxel and Oxaliplastin, were totally (100%) compliant with their medications. Major reasons for medication non-adherence with oral cancer chemotherapy were forgetfulness (18.9%) and carelessness about time to take medications (14.1%). Significant ($p < 0.05$) factors and attitudes associated with medication adherence were gender, number of medications per day, forgetting to take medications, not knowing how and when to take medications, checking name and dosage before taking medication, and storing medications in an appropriate place. Overall, the patients had above-average adherence to their oral antineoplastic therapy, but experienced difficulty in treatment with a positive Morisky green Test score.

INTRODUCTION

There is a global increase prevalence of cancer with a higher projection in developing countries [1], and it is one of the main causes of death [2]. About 20 million people worldwide in 2022 were newly diagnosed of cancer [3]. The National Cancer Control Plan (2018-2020) reported an annual estimate of 102,000 new cases of cancer, and 72,000 deaths recorded in Nigeria, among which breast cancer was ranked highest [4, 5]. Due to rising industrialization and westernization of nutrition and other socio-behavioral attitudes in many developing countries, it is anticipated that cancer will reach pandemic proportions in the twenty-first century [6]. The burden of cancer can be reduced by identification of risk factors, screening, early diagnosis, treatment and palliative care [7].

Medication adherence is defined as "taking medication as prescribed regarding the daily amount, dosage, and frequency", and persistence refers to "the duration of time from initiation to discontinuation of therapy" [8]. The efficacy

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of disease management frequently depends on adherence to a specified drug regimen. [9]. Non-communicable diseases are anticipated to account for more than 65% of all disease burden, however 50–60% of patients fail to follow their doctors' recommended treatment plans [10]. Of the antineoplastic medications often prescribed, only very few are oral chemotherapy [11], and the number of oral anti-neoplastic therapies are now recently on the increase [12], of which adherence is of major concern [13, 14]. Non-adherence to oral antineoplastic medications is highly associated to poor disease outcomes, such as higher risk of treatment resistance, early disease progression or recurrence, and premature death [15, 16].

Prescribers of anticancer drugs might assume that patients with severe diseases, like cancer, take their medication as prescribed [13, 17]. However, recent studies have shown that adherence to anticancer drug treatment is a serious problem with a reported adherence rate between 16% and 100% [18]. Adherence to chemotherapy in developing countries is poor when compared to developed nations [19, 20]. To achieve optimum therapeutic outcomes for cancer patients, adherence is expected to be near total (100%) [11, 21]. On the other hand, insufficient medication adherence can result in treatment failure, disease progression, a reduction in the quality of life and increasing care burden for cancer patients [22]. Previous studies in Nigeria only reported adherence among breast cancer patients [23 – 25]. Despite the various barriers and challenges faced by cancer patients regarding medication adherence, there is little or no information on adherence to antineoplastic regimens among all cancer patients in Nigeria. The study aimed to assess medication adherence and the attitude of cancer patients to anti-neoplastic therapy in a tertiary hospital, in Benin City, Nigeria.

MATERIALS AND METHODS
Study Design and Setting
The study was a cross-sectional prospective survey to evaluate medication adherence and the attitude of cancer patients to anti-neoplastic therapies in a tertiary hospital, in Benin City. The study was carried out at the oncology unit of the University of Benin Teaching Hospital (UBTH), Benin City. It is a tertiary multi-specialty healthcare facility in Edo State, Nigeria, which renders specialized healthcare services as well as **a** main referral centre to the people of the state and other neighbouring states such as Delta, Ondo and Kogi States. It has a bed space capacity of over 900 as of August 2019.

Study Participants and Sampling
The study was conducted from March to April, 2022. Participants included male and female, 18 years and above, already diagnosed cancer out-patients, who have been on anti-neoplastic medications for not less than 6 months before the study, and willing to participate in the study. Those who were terminally ill, and other cancer in-patients, and those who failed to complete the survey instrument were excluded

from the study. A convenient sampling method was used for all diagnosed cancer patients, who were on routine medical visits to the oncology unit, as well as those who came for their refill medications at the Pharmacy. Out of a total of 110 diagnosed cancer patients, 90 were conveniently sampled, and participated in the study, giving an 81.8% response rate.

Data Collection
Data was collected using a self-developed instrument, and Morisky and Green Test (MGT) questionnaire [26]. The instruments consist of demographics and clinical information (age, sex, diagnosis, duration of illness, chemotherapeutic agents, as well as number of medications). MGT evaluates patients' adherence and attitude towards treatment, it comprises four adherence questions with Yes = 0 and No =1 answers, and factors or attitudes that may affect patient treatment compliance which is made up of seventeen 5-Likert scale questions, totally agree, partly agree, indecisive, partly disagree or totally disagree, with values of 5, 4, 3, 2 and 1 respectively, with scores ranging between 17 to 85.

Data Analysis
Data was analyzed using Statistical Package for Social Sciences (SPSS) version 27, and GraphPad InStat version 3. The analyses were both descriptive and inferential. Adherence score of 3 to 4 was considered as good adherence, and a score of $\leq$ 2 was seen as poor or non-adherence. Scores for attitude to treatment were reverse coded with a minimum score of 17 and a maximum score of 85. An attitude score of $\leq$ 3.5 was considered a positive attitude with treatment, having little or no difficulty to treatment, while an attitude score of more than a mean score of >3.5 was considered as a poor attitude and having difficulty with treatment. Fischer exact test was done to compare adherence and non-adherence to oral cancer therapy, and also to determine the association of patient characteristics of the respondents to medication adherence. Results were considered significant at $p < 0.05$. Outcome measures were medication adherence, attitude to treatment and medication use.

Ethical Considerations
Approval for the study was sought and obtained from the Ethics Committee of UBTH with protocol number ADM/E 22/A/VOL VII/14830196. Written and oral informed consents were obtained from the studied participants; confidentiality of information was guaranteed

RESULTS
Patients' Social and Clinical Characteristics
Almost one-third (31.1%) of the respondents were within the age range of 56 – 65 years, and the majority (63.3%) were female, with most (73.3%) of them married with children (86.7%). Less than half (41.1%) had up to tertiary education, and very many (95.5%) of them were Christian by religion.

Table 1: Patients' sociodemographic and clinical characteristics

Variables	Frequency	Percentage
Age category (Years)		
26 – 35	10	11.1
36 – 45	11	12.2
46 – 55	27	30
56 – 65	28	31.1
Above 65	14	15.6
Gender		
Male	33	36.7
Female	57	63.3
Marital status		
Single	14	15.6
Married	66	73.3
Divorced	10	11.1
Educational level		
No formal education	5	5.6
Primary	10	11.1
Secondary	37	41.1
Tertiary	37	41.1
Others	1	1.1
Religion		
Christianity	86	95.5
Islam	2	2.2
Others	2	2.2
Family income		
Less than ₦50,000	20	22.2
₦50,000 - ₦70,000	27	30
₦71,000 - ₦100,000	27	30
Above ₦100,000	16	17.8
Do you have any children?		
Yes	78	86.7
No	12	13.3
Number of children		
None	12	13.3
1 -3	41	45.6
4 – 6	25	27.8
7 – 10	11	12.2
Above 10	1	1.1
Do you have any siblings?		
Yes	84	93.3
No	6	6.7
Number of siblings		
None	5	5.6
1 -3	37	41.1
4 – 6	28	31.1
7 – 10	16	17.8
Above 10	4	4.4
Family history		
Yes	28	31.1
No	62	68.9
Diagnosis (cancer)		
Breast	28	31.1
Prostate	18	20.0
Cervical	17	18.9
Colorectal	4	4.4

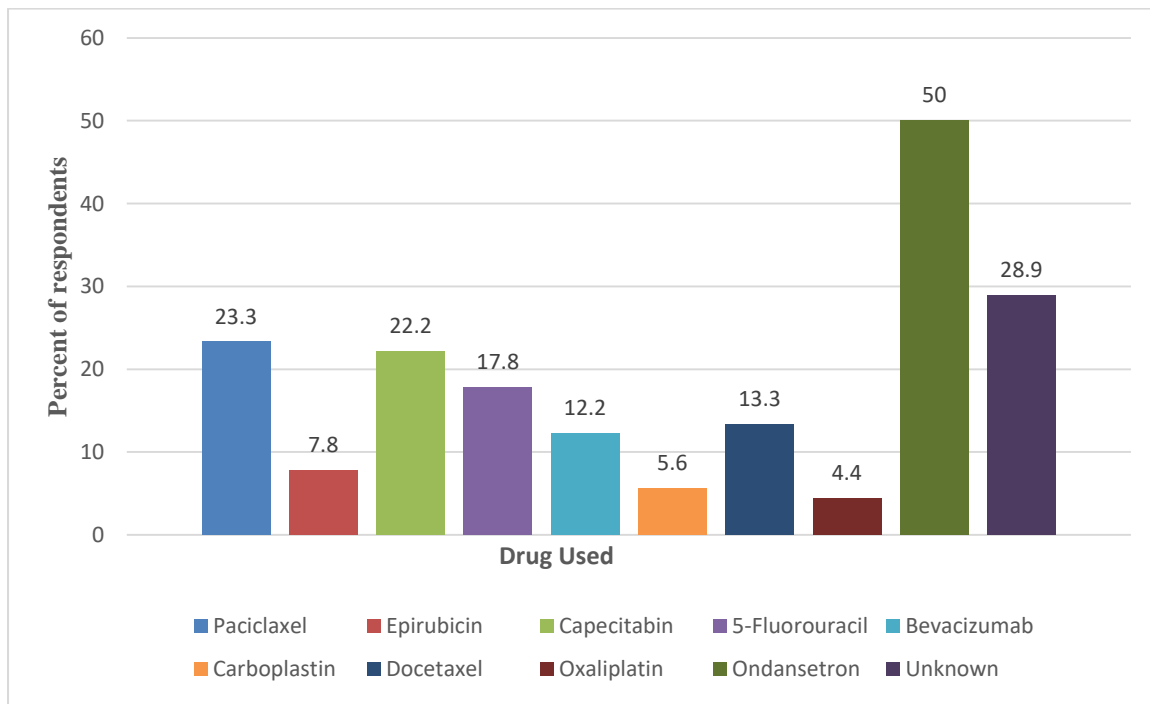|		
Non-melanoma skin	6	6.7
Liver	3	3.3
Ovary	4	4.4
Others	10	11.1
Duration of illness		
6 – 12 months	62	68.9
1 – 5 years	25	27.9
5 – 10 years	3	3.3
Number of medications per day		
1 – 2	33	36.7
3 – 5	51	58.7
6 – 8	6	6.7

Figure 1: Antineoplastic medication use by the respondents.

Table 2: Medication adherence to oral antineoplastics among cancer patients

Morisky-Green test	Yes		No		P value
	N	%	N	%	
Have you ever forgotten to take your medication?	17	18.9	73	81.1	
Are you sometimes careless with time to take your medication?	13	14.1	77	85.6	
When you feel good, don you quit taking medication?	5	5.6	85	9 4.4	
When the medication makes you feel sick, do you abandon it?	8	8.9	82	91.1	
Adherence level					**0.0001***
Adherence	62	74.4			
Non-adherence	28	25.6			
Morisky-Green Test	**Positive**		**Negative**		
	23	**25.6**	**67**	**74.4**	**< 0.0001***
Oral antineoplastic medication					0.08
Paclitaxel	5	23.8	16	76.2	

Epirubicin	3	42.9	4	57.1
Capecitabine	2	10.0	18	90.0
5-fluorouracil	7	46.7	8	53.3
Bevacizumab	0	0	11	100
Carboplastin	2	20.0	3	80.0
Docetaxel	0	0	4	100
Oxaliplatin	0	0	4	100
Ondansetron	11	24.4	34	75.6
Unknown	8	30.8	18	69.2

Table 3: Level of agreement with factors and attitudes that may affect compliance to antineoplastic treatment

Factors and attitude	Completely disagree (1) N (%)	Partially disagree (2) N (%)	Indecisive (3) N (%)	Partially agree (4) N (%)	Completely agree (5) N (%)	Mean score
1. Medication causes undesirable effects	11 (12.3)	3 (3.3)	6 (6.7)	13 (14.4)	57 (63.3)	4.13±1.39
2. I forget to take medication	57 (63.3)	4 (4.4)	0 (0)	22 (24.4)	7 (7.8)	2.09±1.53
3. I need help to take medication	50 (55.6)	3 (3.3)	1 (1.1)	26 (28.9)	10 (11.1)	2.37±1.62
4. I have to take a lot of medication	8 (8.9)	27 (30.0)	2 (2.2)	3 (3.3)	50 (55.6)	3.67±1.58
5. I do not know how to take medication	70 (77.8)	6 (6.7)	0 (0)	10 (11.1)	4 (4.4)	1.58±1.21
6. Oral medication is complicated	48 (53.3)	6 (6.7)	3 (3.3)	29 (32.2)	4 (4.4)	2.28±1.48
7. I have difficulty to remember day to take medication	61 (67.8)	8 (8.9)	2 (2.2)	12 (13.2)	7 (7.8)	1.84±1.39
8. I have difficulty to buy medication	18 (20.0)	4 (4.4)	2 (2.2)	8 (8.9)	58 (64.4)	3.93±1.63
9. I do not know when to take medication	58 (64.4)	7 (7.8)	4 (4.4)	11 (12.2)	10 (11.1)	1.98±1.48
10. Medication is hard to swallow	56 (62.2)	8 (8.9)	0 (0)	19 (21.1)	9 (10.0)	2.10±1.54
11. I forget to attend consultations	79 (87.8)	4 (4.4)	1 (1.1)	0 (0)	6 (6.7)	1.33±1.03
12. Oral medication treatment causes fewer job absences	44 (48.9)	7 (7.8)	13 (14.4)	7 (7.8)	19 (21.1)	2.44±1.67
13. Health team has helped with oral medication treatment.	7 (7.8)	2 (2.2)	2 (2.2)	1 (1.1)	78 (86.7)	4.57±1.17
14. I have specific hours to take medication	6 (6.7)	2 (2.2)	0 (0)	13 (14.4)	69 (76.7)	4.52±1.09
15. I check name and dosage before taking medication	5 (5.6)	7 (7.8)	3 (3.3)	6 (6.7)	69 (76.7)	4.41±1.21
16. I store medication in an appropriate place	2 (2.2)	1 (1.1)	3 (3.3)	6 (6.7)	78 (86.7)	4.74±0.77
17. I take medication even when I am sick	7 (7.8)	12 (13.3)	2 (2.2)	8 (8.9)	61 (67.8)	4.16±1.39
Overall mean						3.07±1.22

Table 4: Factors and attitude associated with medication adherence

Variables/Factors, attitude	Non-adherence N (%)	Adherence N (%)	P value
Marital status			0.024
Single	2 (14.3)	12 (65.7)	
Married	15 (22.7)	51 (77.3)	
Divorced	6 (60)	4 (40)	
Number of medications per day			0.013
1 – 2	14 (42.4)	19 (57.6)	
3 – 5	9 (17.7)	42 (82.3)	
6 – 8	0 (0)	6 (100)	
Forget to take medication			<0.00001
Completely disagree	4 (7.0)	53 (93.0)	
Partially disagree	2 (50)	2 (50)	
Partially agree	11 (50)	11 (50)	
Completely agree	6 (85.7)	1 (14.3)	
Don't know how to take medication			0.004
Completely disagree	14 (20.0)	56 (80.0)	
Partially disagree	2 (33.3)	4 (66.7)	
Partially agree	3 (30.0)	7 (70.0)	
Completely agree	4 (100)	0 (0)	
Don't know when to take medication			0.039
Completely disagree	11 (19.0)	47 (81.0)	
Partially disagree	1 (14.3)	6 (85.7)	
Indecisive	3 (75.0)	1 (25.9)	
Partially agree	3 (42.1)	8 (72.7)	
Completely agree	5 (50)	5 (50)	
Oral medication treatment causes fewer job absences			0.02
Completely disagree	5 (11.4)	39 (88.6)	
Partially disagree	2 (28.6)	5 (71.4)	
Indecisive	7 (53.8)	6 (42.2)	
Partially agree	3 (42.9)	4 (57.1)	
Completely agree	6 (31.6)	13 (68.4)	
The health team has helped with oral medication			0.046
Completely disagree	2 (28.6)	5 (71.4)	
Partially disagree	2 (100)	0 (0)	
Indecisive	0 (0)	2 (100)	
Partially agree	1(100)	0 (0)	
Completely agree	18 (23.1)	60 (76.1)	
Checked name and dosage before taking medication			0.004
Completely disagree	1 (20.0)	4 (80.0)	
Partially disagree	1 (14.3)	8 (85.7)	
Indecisive	3 (100)	0 (0)	
Partially agree	4 (66.7)	2 (23.3)	
Completely agree	14 (20.3)	55 (79.7)	
Store medication in an appropriate place			0.001
Completely disagree	0 (0)	2 (100)	
Partially disagree	1 (100)	0 (0)	
Indecisive	3 (100)	0 (0)	
Partially agree	4 (66.7)	2 (33.3)	
Completely agree	15 (19.2)	63 (80.a8)	

Where p <0.05 is statistically significant

Most (82.2%) of the respondents lived below a family income of less than or equal to ₦100,000. A few (31.1%) of them had a family history of cancer, with breast cancer (31.1%) being the highest diagnosis, closely followed by prostate (20.0%) and cervical (18.9%) cancer respectively. The majority (68.9%) of the respondents were diagnosed with cancer between 6 to 12 months, and 65.4% took more than two forms of medications (Table 1).

Antineoplastic Medication Use by the Respondents
The antineoplastic drugs mostly prescribed was ondansetron (50.0%) which was closely followed by paclitaxel (23.3%), capecitabine (22.2%) and 5-fluorouracil (17.8%). However, 28.9% of the patients were unaware of their medication (Figure 1).

Medication Adherence to Oral Antineoplastics Among Cancer Patients
The medication adherence to oral antineoplastics is shown in Table 2. The majority (74.4%) of the respondents adhered to their antineoplastic medication which was statistically significant ($P < 0.05$), but a few (25.6%) of them had a positive Morisky and Green Test score, and was also statistically significant ($P < 0.05$). Major reasons for non-adherence to antineoplastic medications were forgetfulness (18.9%) and carelessness (14.1%) with time to take medication. There was a significant ($P > 0.05$) difference between the Morisky and Green Test and the types of medication used. Patients who used Paclitaxel, Epirubicin, Capacitabine, 5-fluoroural, Carboplastin and Oendansetron had a positive MGT, thus were not compliant, while those using Bevacizumab, Docetaxel and Oxaliplastin, were compliant with their medications.

Level of Agreement with Factors and Attitudes that may affect Compliance to Antineoplastic Treatment
Major positive attitudes contributing to little or no difficulty in treatment (mean score ≤ 3.5) were; forgetting to take medication, needing help to take medication, not knowing how to take medication, oral medication is complicated, having difficulty to remembering day to take medication etc., (Table 3). Overall the respondents had a positive attitude and little or no difficulty in treatment with a total mean score of 3.07±1.22.

Factors and Attitude Associated with Medication Adherence
The factors associated with medication adherence are as shown in Table 4 below. Marital status, number of medications, forgetfulness, not knowing how and when to take medications, checking name and dosage before taking medication, and storing medications in an appropriate place. These were all significantly associated with $P < 0.05$.

DISCUSSION
This study's main findings revealed that most of the patients adhered to their antineoplastic medications, but only a few had a positive attitude to treatment with difficulty to treatment. Forgetfulness and carelessness with time to take medications were major barriers to adherence to antineoplastic medications. Similarly, some of the significant factors and attitudes associated with medication adherence were gender, number of medications per day, forgetting to take medications, not knowing how and when to take medications, checking name and dosage before taking medication and storing medications in an appropriate place.

There were more females than males diagnosed with cancer in this study, this is consistent with a previous study in south-western Nigeria [5], but opposed to a study in Nepal, which observed a higher prevalence of cancer among males [27]. This may be because females are more conscious of their health, which may eventually lead to more clinic attendance. This could also be due to a higher incidence of breast and cervical cancer reported in this study. Studies in developed countries and Nigeria also reported higher cases of breast cancer [3, 5].

It was also established in the study, that married status was more implicated with cancer. This is in agreement with other studies, which reported an association of breast and cervical cancer with childbearing and sexual intercourse [28, 29]. Married participants were also found to adhere to antineoplastic medications. This is so because their spouse can give social and emotional support to their partner which could help to improve adherence to medications.

Most (74.4%) of the respondents in this study, reported above-average adherence to their antineoplastic medications. This is higher than previous studies in Nigeria and Japan, which observed an adherence of 19.1% and 56.4% respectively [23, 30], but lower than studies carried out in the Unted States and Brazil, which reported an adherence rate of 85.6% and 85.2% respectively [31, 32]. The high rate of medication adherence observed in this study may largely be attributed to the severity of the disease, which could positively influence adherence to oral antineoplastic drugs, and also due to greater belief in and reliance on health professionals. Previous research reports, that adherence to medication and treatment satisfaction may be improved, due to patient's expectations and views regarding their doctor and the medical staff [33, 34].

Major reasons for non-adherence to antineoplastic medications were forgetfulness (18.9%), a result which is similar to previous studies which reported forgetting to take medications and other factors as limitations to adherence [35, 36]. Similarly, the number of medications taking per day was one of the significant associated factors or attitudes affecting medication adherence in this study. It was observed that most patients took between 3 - 5 medications per day, an indication that the higher the number of oral antineoplastic drugs taken, the less likely they adhere to medications prescribed. Polypharmacy has been found to hinder medication

adherence [37 - 39], which in turn may contribute to a high incidence of adverse effects and increased cost of antineoplastic drugs. In Nigeria, due to a lack of financial support and limited resources, patients may be faced with the challenge of non-adherence to medications. In this study however, of the number of patients that adhered to their antineoplastic medications, 88.6% of them completely disagreed that oral medications cause fewer job absences, indicating that they can cope with the associated adverse effects of these drugs. Previous studies have found a relationship between adverse drug effects with treatment compliance [30, 40, 41]. In addition, the belief that health teams have helped with oral medication observed in this study has also contributed to adherence to medication. This is an indication that patients were more satisfied with the types of care offered by the health team.

The study is however without limitations; The study was a cross-sectional, and was carried out in a single health facility, as such, findings cannot be generalized. Further studies involving multi center health facilities are hereby suggested. The reports of medication adherence by the participants recorded in this study, may have been overestimated, this is because information was self-reporting, and may not be free from recall bias. Other variables such as disease staging and severity, social support and motivation for the patients that may affect adherence, were not assessed in this study.

CONCLUSION

In this study, although patients had above-average adherence to their oral antineoplastic therapy, adherence was below the expected optimum 85% for patients on oral cancer chemotherapy. There was a positive Morisky Green Test score of 25.6%, an indication of non-compliance. Patients were highly satisfied with the treatment and services offered by the health professionals. Major barriers to medication adherence were forgetfulness, and time to take medications. Evaluating patients' adherence will facilitate effective treatment plans and satisfaction among health professionals.

CONFLICT OF INTEREST

There were no conflicts of interest whatsoever in the course of the study

AUTHORS' CONTRIBUTION

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