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ABSTRACT

Objectives Prime focus of this study was to evaluate the availability and affordability of originator brands (OBs) and lowest price generics (LPGs) of prescribed biologic and non-biologic anticancer medicines.

Design, settings and participants A descriptive, cross-sectional survey was conducted in 22 cancer-care hospitals (18 public hospitals and 4 private hospitals) and 44 private pharmacies in Punjab, Pakistan. Sampling population consisted of 4483 patients with cancer aged ≥18 years. The availability was determined by classifying anticancer medicines in four categories: absent/unavailability (medicines not present in any surveyed facility), low availability (medicines present in <50% of surveyed facilities), fairly high availability (medicines present in 50%–74% of surveyed facilities) and high availability (medicines present in >75% of surveyed facilities). Medicines were affordable if overall cost of all the prescribed anticancer medicines were 20% of the household capacity to pay. Data were analysed by using Statistical Packages for Social Sciences (IBM SPSS Statistics for Windows, V.21.0).

Results A total of 5060 patients with cancer were approached out of which 4483 patients were included in the survey. Overall, 10103 anticancer drugs were prescribed. Among them, 96.3% were non-biologics and 3.7% were biologics. Oncologists were reluctant to prescribe biologics due to high prices. 58.1% of non-biologics were affordable; whereas, the affordability of biologics was 3.3%. A total of 43.9% of both biologic and non-biologic OBs were available; whereas, their affordability was 44.2%. On the other hand, the availability of LPGs was 21.3%, and their affordability was 66.1%. For low-income patients, the affordability of non-biologics was 31.6% and the affordability of biologics was 1.1%.

Conclusions Most of the patients with cancer were prescribed non-biologics due to their low price and better affordability. In contrast to OBs, LPGs of both biologics and non-biologics had less availability but more affordability.  

INTRODUCTION

Cancer is one of the most lethal non-communicable diseases. The advancement in medical and pharmaceutical sciences has resulted in a wide range of therapeutic options for treating this disease that mainly includes non-biologic and biologic anticancer medicines.1 According to Food and Drug Administration (FDA), biologics are made up of protein, sugar or nucleic acid or their complex combination or may be living entities (eg, tissues and cells). These are isolated from biological origin and produced by using cutting-edge techniques and biotechnological processes.2 The major issue in using non-biologic or chemotherapeutic agents is the non-specific killing of cells. The approval of rituximab by FDA as a first biologic agent for treating cancer led to a new era of anticancer drugs in 1997.3 The greater efficacy and decreased toxicity has made biologics superior. In contrast to conventional non-biologics, biologic medicines have proven to improve the survival rates and patient’s quality of life.4 However, the substantial cost of biologics is a source of huge financial encumbrance for the patients. According to an estimate the average per-month cost of anticancer medicines has increased by more than two folds (ie, from $4500 to >$10 000 in the last decade).5 6 In 2007, the American Society of Clinical Oncology has established
a task force to identify the factors responsible for high prices of anticancer medicines.\textsuperscript{7}

Worldwide, there is a dearth of availability of anticancer drugs at affordable prices. In many regions of the world, the affordability is defined as the costs which do not pose a financial encumbrance on patients. The high prices of biologics and non-biologics among different regions of the world and non-availability of lowest price generics (LPGs) particularly for biologics are the root causes of this economic burden.\textsuperscript{8} Since the patients in low/middle-income countries (LMICs) find it difficult to afford non-biologics, their treatment with new therapeutic agents like biologic is almost impossible. Therefore, the management of cancer is seriously affected by the availability and affordability of anticancer agents.\textsuperscript{9}

Some probable reasons which might hinder the accessibility of LPGs may include the reimbursement, budget allocation, manufacturing processes, patent rights, data exclusivity and bioequivalent studies.\textsuperscript{4,10-13} Also, ‘mark-up values’ by the hospitals, wholesale dealers, pharmacists and physicians may contribute in making the prices extremely high.\textsuperscript{14,15} Moreover, a preapproval is needed for the provision of subsidised medicines. This may cause poor access towards therapeutic agents, and it ultimately leads to a considerable delay in the commencement of treatment.\textsuperscript{16} Consequently, recovery of patients is negatively affected. A study by the Association of Oncology Social Work has reported symptoms of anxiety and depression among patients with cancer due to the economic burden associated with cancer treatment.\textsuperscript{12}

The poor availability and affordability of anticancer drugs is a common issue in Pakistan. There are evidences that depict the formulary limitation and resource allocation as the major causes for this drastic issue. The shortage of anticancer drugs and unavailability of formulary for these agents are due to weak healthcare system and poor collaboration of healthcare professionals. The improper allocation of budget also makes the anticancer drugs especially biologics unaffordable for both government and local masses.\textsuperscript{7,17} If the anticancer medicines are unavailable or unaffordable for the patients then it would not only aggravate their underlying disease but it would also lead to the inequities between the patients who can get them versus those who fail to get access to those medicines.

The WHO and the Health Action International (HAI) have given a standard methodology for evaluating affordability\textsuperscript{18} and numerous studies focusing on the gravity of underlying problem have been conducted in multiple countries. However, affordability in the current study has not been evaluated by this method because anticancer medicines are quite expensive, and the WHO and HAI methodology does not fit true for anticancer medicines. It is crucial to determine the method in the context of the country and the medicine class.\textsuperscript{19} To date, no study has been conducted to find out the affordability of anticancer medicines, and it demands formulating the appropriate method/formula for determining the affordability of anticancer medicines. The aim of the current study is to assess the availability of biologic and non-biologic anticancer medicines in public and private sectors, and their affordability by high-income, middle-income and low-income class patients.

 METHODS
Study design and settings
A descriptive, cross-sectional study design was employed. There are total 23 (18 public and 4 private sector tertiary care) hospitals in Punjab province of Pakistan which provide services to patients with cancer. Out of these 23 hospitals, 7 are specialised cancer-care hospitals. Except for one hospital (which provides services solely to the paediatrics), all the hospitals providing services to patients with cancer in Punjab province of Pakistan were included in the current study. Survey was carried out in 22 cancer-care hospitals and 44 private pharmacies in Punjab province of Pakistan. Data were collected from patients with cancer attending the study settings and evaluated according to the objectives of the study.

Study population and sample size
The population under study was patients with cancer aged ≥18 years, who visited the selected cancer-care hospitals for routine examinations. A total of 200 patients with cancer were randomly approached from each hospital, thus leading to a sample size of 4400. However, with the contingency of 15% for non-response and inappropriate responses, the sample size was 5060.

A total of 5060 patients with cancer were approached over a 6-month period (1 January 2017 to 30 June 2017), out of which 4613 patients responded to the survey (response rate=91.2%). The remaining patients were not willing to participate in the study due to several reasons such as illiteracy, superstitions, shortage of time due to household responsibilities and previous worse experiences. Out of 4613 patients with cancer 130 had missing information, therefore they were excluded from the study. Thus, 4483 patients with cancer were finally included in the survey.

Data collection and outcome variables
A data collection form was designed for this study which consisted of three main parts: (1) sociodemographic characteristics, (2) diagnosis and (3) recommended medicines. The reliability and internal consistency of the survey tool were assessed by conducting a pilot study. Piloting was undertaken using data from 100 patients. The data were collected only once from the study settings. There was no repetition of interviews or visits.

Measurements
Sociodemographic characteristics
The following categorical variables were recorded: gender (male/female), age (18−39, 40−64, ≥65 years), civil status (single, married, divorced, widowed), education level (primary, secondary, tertiary), annual income
(low, middle, upper class), residence (rural, urban) and employment status (employed, unemployed). The retired participants (taking pension) or those running a business were classified as employed and housewives were considered as unemployed. The data were obtained through face-to-face questioning of patients. The data on annual income were determined from Household Integrated Economic Survey 2016 conducted by Pakistan Bureau of Statistics. Detailed investigation about household possessions, average monthly household income, average monthly household consumption and per-capita monthly consumption expenditure was carried out for evaluating their socioeconomic status. As in Pakistani cultural context women did not know the income of the family, all the data were verified from the head of their family. The data regarding employment status and income level of the participants were validated by using online tax payer verification system of Federal Board of Revenue.

Diagnosis and prescribing pattern
The type of cancer and all the medicines prescribed to patients were noted on a predesigned pro-forma sheet. The most commonly prescribed anticancer medicines were categorised according to the prescribing trend; low (prescribed to <5% of the selected patients), medium (prescribed to ≥5% of the selected patients but <10%) and high (prescribed to >10% of the selected patients).

Availability of anticancer medicines and their per month cost
Fifty anticancer medicines were recorded in the survey. Biologics other than protein kinase inhibitors and monoclonal antibodies were not evaluated in the study since they were not prescribed to the selected patients. The anticancer medicines were selected on the basis of: (a) pilot study in which local needs and cancer burden were assessed, (b) literature review and (c) the opinions of various experts. The medicines were considered available if they were present at the study setting during the survey. The availability of anticancer medicines was evaluated in public hospitals, private hospitals and private pharmacies. For the assessment of prices associated with these medicines, Pharmaguide 2016 was consulted. Data collection was carried out by trained pharmacy students under the supervision of the survey manager and the principal investigator. The principal investigator checked the collected and completed pro formas on a weekly basis. A follow-up visit to the respective setting was conducted in case any information was missing. Before the initiation of the process of data collection, medical superintendents/directors were contacted by the principal investigator. In this way, a good cooperation was established between the team of investigators and the staff members of the selected settings. To avoid reporting biases (eg, up coding, less availability of medicine to gain attention for budget increase, etc), the drugs were said to be available if they were present in the settings, and the patients could avail them on prescription. Also, the formulary list and purchase records were assessed for data validation. For each medicine, data were collected on the basis of per-unit price and availability of originator brands (OBs) and LPGs. On the basis of standard guidelines and the recommended treatment, per-unit price of anticancer agents were transformed into per-month cost.

Furthermore, the following criteria were used to describe the availability of medicines:

- **Absent/unavailability**: 0% of facilities—these medicines were not found in any facility surveyed.
- **Low**: <50% of facilities—these medicines were hard to find.
- **Fairly high**: 50%–74% of facilities—these medicines were available in many facilities.
- **High**: >75% of facilities—good availability.

Affordability of anticancer medicines
The WHO and HAI methodology states that the income of how many days is required to purchase the medicines for 30 days needs to be determined for evaluating affordability. Generally, if the total cost of therapy for 1 month is equal to or less than the wage of 1 day then it is said to be affordable.

The method used in current study for assessing affordability is not validated from the previously published literature. But the expert opinion of researchers and policy-makers was taken into consideration while designing this methodology. The concept of cut-off value by Khatib et al is defined as ‘if the combined cost of therapy is <20% of household capacity-to-pay then it can be considered as affordable’. In this study, this concept was modified in such a way that the medicines were affordable if overall cost of all the prescribed anticancer medicines were 20% of the household capacity to pay. The affordability was measured for each prescribed medicine by low-income, middle-income and high-income class of patients through this formula:

\[
\text{Affordability} = \left( \frac{\text{Per month cost of the medicine}}{\text{Per month cost of household capacity to pay}} \right) \times 100
\]

*If one medicine was prescribed then it was said to be affordable if it covers 20% of the household capacity to pay, if two medicines were prescribed then they were said to be affordable if each of them covered 10% of the household capacity to pay, if three medicines were prescribed then they were said to be affordable if each of them covered 6.7% of the household capacity to pay and if four medicines were prescribed then they were said to be affordable if each of them covered 5% of the household capacity to pay.*

Statistical analysis
Statistical Package for Social Sciences (IBM, SPSS Statistics for Windows, V.21.0) was used for data analysis. Descriptive statistics such as frequencies, percentages and mean were used to present the data.
Patient and public involvement

The poor availability and affordability of anticancer medicines is a common issue in Pakistan, and the research question was in line with the priorities and preferences of patients with cancer. The purpose of the study was explained to all the patients prior to the study being conducted. They were informed that it was a descriptive, cross-sectional study in which there would be neither any intervention nor follow-up, and their confidentiality would not be breached. Data were collected by recruiting patients with cancer in the study and evaluating them according to the objectives of the study. The results would be disseminated to study participants by contacting them at their respective email addresses.

RESULTS

A total of 5060 patients with cancer were approached, out of which 4483 patients were included in the survey. Just over half (55.4%, n=2485) of the participants were male, and 39.3% (n=1768) were aged 18–39 years; 67.5% (n=3029) were married, 67.4% (n=3023) had secondary education level and 41.8% (n=1874) belonged to the upper class; 68.7% (n=3080) respondents were employed and three-quarters (73.7%, n=3302) were urban residents (table 1).

The most common cancers diagnosed among participants were non-Hodgkin’s lymphoma (12.2%, n=545), breast cancer (8.5%, n=380) and leukaemia (7.6%, n=339) (online supplementary file).

A total of 10 103 anticancer medicines were prescribed to 4483 patients. Among them, 96.3% (n=9729) were non-biologics. Other antineoplastic agents (31%, n=3007) and antimetabolites (21.5%, n=2089) were the most frequently prescribed groups of non-biologic anticancer medicines. Overall, only 3.7% (n=374) of the patients were prescribed biologics. Among them, 94.3% (n=353) were prescribed protein kinase inhibitors while 5.6% (n=21) were prescribed monoclonal antibodies. The detailed description about the prescribed anticancer medicines is given in table 2.

Availability of OBs and LPGs

Overall, OBs (43.9%) were readily available in all the selected settings compared with LPGs (21.3%). The high availability of all the anticancer medicines was found in private sector (OBs=62.5%, LPGs=15.6%) compared with public sector (OBs=25.1%, LPGs=8.8%) (table 3).

Availability of non-biologics and biologics

Non-biologics (OBs=52.8%, LPGs=24.3%) were more readily available compared with biologic anticancer medicines (OBs=12.3%, LPGs=0.0%). The availability of both non-biologic and biologic agents was found to be more in private sector compared with public sector (table 3).

Affordability of OBs and LPGs

OBs (44.2%) of all the anticancer medicines were found to be less affordable than LPGs (66.1%); however, their affordability varied among different income classes. OBs were more affordable (59.2%) for high-income class patients, less (40.4%) for middle-income patients and least (24.1%) for low-income patients (table 4).

Affordability of biologics and non-biologics

Irrespective of the OBs and LPGs, non-biologics (58.1%) were more affordable than biologics (3.3%). Also, non-biologics (31.6%) were more affordable for low-income patients than biologics (1.1%) (table 4).

Table 1 Characteristics of the study population

| Variables                  | Male (n=2485) | Female (n=1998) | Total (n=4483) |
|---------------------------|--------------|----------------|---------------|
| Age (years)               |              |                |               |
| 18–39                     | 984 (39.6)   | 784 (39.2)     | 1768 (39.4)   |
| 40–64                     | 794 (31.9)   | 880 (44.0)     | 1674 (37.3)   |
| ≥65                       | 707 (28.5)   | 334 (16.7)     | 1041 (23.2)   |
| Civil status              |              |                |               |
| Single                    | 108 (4.4)    | 60 (3.0)       | 168 (3.8)     |
| Married                   | 1747 (70.3)  | 1282 (64.2)    | 3029 (67.6)   |
| Widowed                   | 370 (14.9)   | 514 (25.7)     | 884 (19.7)    |
| Divorced                  | 260 (10.5)   | 142 (7.1)      | 402 (8.9)     |
| Education level           |              |                |               |
| Primary (≤10 years)       | 503 (20.2)   | 0 (0.0)        | 503 (11.2)    |
| Secondary (11–13 years)   | 1414 (56.9)  | 1609 (80.5)    | 3023 (67.4)   |
| Tertiary (≥14 years)      | 568 (22.9)   | 389 (19.5)     | 957 (21.4)    |
| Annual income (PKR)       |              |                |               |
| Low class (0–299 999)     | 662 (26.6)   | 481 (24.1)     | 1143 (25.5)   |
| Middle class (300 000–999 999) | 842 (33.9) | 624 (31.2) | 1466 (32.7) |
| Upper class (≥1 000 000)  | 981 (39.5)   | 893 (44.7)     | 1874 (41.8)   |
| Employment status         |              |                |               |
| Employed                  | 2187 (88.0)  | 619 (30.9)     | 3080 (68.7)   |
| Unemployed                | 298 (11.9)   | 1379 (69.9)    | 1677 (37.4)   |
| Residence                 |              |                |               |
| Rural                     | 855 (34.4)   | 326 (16.3)     | 1181 (26.3)   |
| Urban                     | 1630 (65.6)  | 1672 (83.7)    | 3302 (73.7)   |
| Number of medicines       |              |                |               |
| 1                         | 79 (3.2)     | 164 (8.2)      | 243 (5.4)     |
| 2                         | 1781 (71.7)  | 1213 (60.7)    | 2994 (66.8)   |
| 3                         | 571 (22.9)   | 541 (27.1)     | 1112 (24.8)   |
| 4                         | 54 (2.2)     | 80 (4.0)       | 134 (2.9)     |

PKR, Pakistani rupee.
### Table 2: Anticancer medicines prescribed to study participants

| Sr. No | Medicine and dose          | ATC code | f (n=10103) %* | OB (manufacturer/importer) | t† (n=6666) | Per-month cost (US$) | LPG (manufacturer/importer) | f§ (n=3537) | Per-month cost (US$) |
|--------|----------------------------|----------|----------------|-----------------------------|-------------|----------------------|-----------------------------|-------------|---------------------|
| (A) Non-biologics (96.3%, n=9729) |
| (i) Alkylating agent (10.6%, n=1026) |
| 1 | Cyclophosphamide 500 mg inj | L01AA01 | 877 (19.6) | High | Cyclomide (Pharmedic) | 619 (13.8) | 50.9 | Cyclophosphamide (S. Ejazuddin) | 258 (5.8) | 27.2 |
| 2 | Ifosfamide 1 g inj | L01AA06 | 71 (1.6) | Low | Ifosfamin (Pharmedic) | 44 (0.9) | 108.7 | Fosfamin (CCL) | 27 (0.6) | 108.7 |
| 3 | Temozolomide | L01AX03 | 4 (0.1) | Low | Temoside (A. J. Mirza) | 4 (0.1) | 561.7 | NA | NA |
| 4 | Dacarbazine 200 mg inj | L01AX04 | 74 (1.7) | Low | Duitcin (Al-Habib) | 36 (0.8) | 24.5 | Darbazine (Pharmedic) | 38 (0.9) | 22.7 |
| (ii) Hormone antagonist (4%, n=388) |
| 5 | Tamoxifen 20 mg tab | L02BA01 | 71 (1.6) | Low | Tamox (Pharmedic) | 49 (1.1) | 5.4 | Tamooxe (Al-Habib) | 22 (0.5) | 4.1 |
| 6 | Bicalutamide 50 mg tab | L02BB03 | 109 (2.4) | Low | Casodex (ICI) | 67 (1.5) | 114.5 | Calutide (A. J. Mirza) | 42 (0.9) | 39 |
| 7 | Anastrozole 1 mg tab | L02BG03 | 71 (1.6) | Low | Anastrozole (Novartis) | 43 (0.9) | 54.4 | Femizet (Atco) | 28 (0.6) | 46.5 |
| 8 | Letrozole 2.5 mg tab | L02BG04 | 71 (1.6) | Low | Femara (Novartis) | 52 (1.2) | 79 | Letara (A.J. Mirza) | 19 (0.4) | 46.2 |
| 9 | Cyproterone Acetate 50 mg tab | G03HA01 | 66 (1.5) | Low | Androcur (Bayer) | 66 (1.5) | 32.5 | NA | NA |
| (iii) Antimetabolite (21.5%, n=2089) |
| 10 | Pemetrexed | L01BA04 | 11 (0.3) | Low | Alimta (Eli Lilly) | 11 (0.3) | 1712.3 | NA | NA |
| 11 | Mercaptopurine 50 mg tab | L01BB02 | 111 (2.5) | Low | Mercaprine (Pharmedia) | 87 (1.9) | 6.7 | Purinethone (Al-Habib) | 24 (0.5) | 5.7 |
| 12 | Fludarabine phosphate 50 mg inj | L01BB05 | 180 (4.0) | Low | Fludara (Sanofi aventis) | 98 (2.2) | 600.8 | Fludakebir (Oncogene) | 82 (1.8) | 420.4 |
| 13 | Cytarabine 100 mg inj | L01BC01 | 342 (7.6) | Medium | Cytosar (Pfizer) | 113 (2.5) | 24.5 | Cytarabine (#Highnoon) | 229 (5.1) | 16.2 |
| 14 | Fluorouracil 500 mg inj | L01BC02 | 502 (11.2) | High | Pharmacur (Pharmedic) | 361 (8.1) | 17.6 | Secouracil (S.Ejazuddin) | 141 (3.1) | 1.6 |
| 15 | Gemcitabine 1 g inj | L01BC05 | 685 (15.3) | High | Gemzar (Eli Lilly) | 402 (8.9) | 580 | Gemita (Atco) | 283 (6.3) | 377.4 |
| 16 | Capecitabine 500 mg tab | L01BC06 | 258 (5.8) | Medium | Xeloda (Roche) | 258 (5.8) | 226.5 | NA | NA |
| (iv) Cytotoxic antibiotics (11.9%, n=1155) |
| 17 | Dactinomycin 0.5 mg inj | L01DA01 | 71 (1.6) | Low | Dactinomycin (Al-Habib) | 12 (0.3) | 259.3 | Dactinofin (Pharmedic) | 59 (1.3) | 213.1 |
| 18 | Doxorubicin 50 mg inj | L01DB01 | 385 (8.6) | Medium | Adriblastina (Pfizer) | 213 (4.8) | 40.7 | Doxorubicin (Al-Habib) | 172 (3.8) | 28.7 |
| 19 | Daunomycin 20 mg inj | L01DB02 | 111 (2.5) | Low | Daunoblastina (Pfizer) | 79 (1.8) | 61.2 | D-Blastin (Pharmedic) | 32 (0.7) | 51.6 |
| 20 | Epirubicin 50 mg inj | L01DB03 | 427 (9.5) | Medium | Farmorubicin (Pfizer) | 223 (4.9) | 120.2 | Anthracin (Atco) | 204 (4.6) | 86.2 |
| 21 | Idarubicin | L01DB06 | 5 (0.1) | Low | Zavedos (Pfizer) | 5 (0.1) | 273.4 | NA | NA |
| 22 | Mitoxantrone 20 mg inj | L01DB07 | 43 (1.0) | Low | Mitoxantrona (Atco) | 43 (1.0) | 36.2 | NA | NA |
| 23 | Bleomycin 15 mg inj | L01DC01 | 42 (1.0) | Low | Bleomycin (Pharmedic) | 31 (0.7) | 90.2 | Bemocin (Atco) | 11 (0.3) | 72.5 |
| 24 | Mitomycin 10 mg inj | L01DC03 | 71 (1.6) | Low | Mitocin (Pharmedic) | 42 (0.9) | 20.4 | Mitomycin (S.Ejazuddin) | 29 (0.7) | 2.1 |

*Values are per month cost (US$) and trend. OB = open batch. Per-month cost (US$): High = >$100, Medium = $50-$100, Low = <$50.
### Table 2

| Sr. No | Medicine and dose | ATC code | f (n=10103) %* | Trend† | OB (manufacturer/importer) | ft (n=6566) | Per-month cost (US$) | LPG (manufacturer/importer) | fj (n=3537) | Per-month cost (US$) |
|--------|-------------------|----------|----------------|--------|---------------------------|-------------|----------------------|-----------------------------|-------------|---------------------|
| (v) Plant alkaloids (20%, n=1949) |
| 25 | Vinblastine 10 mg inj | L01CA01 | 42 (1.0) | Low | Velbastine (Al-Habib) | 19 (0.4) | 37.7 | Vinblas (Pharmedic) | 23 (0.5) | 25.4 |
| 26 | Vincristine 2 mg inj | L01CA02 | 522 (11.6) | High | Pharmacristine (Pharmedic) | 304 (6.8) | 14.3 | Vincristine Gador (Seigror) | 218 (4.8) | 10.2 |
| 27 | Vinorelbine 50 mg inj | L01CA04 | 71 (1.6) | Low | Vinelbine (Alco) | 36 (0.8) | 303.3 | Vinkebir (Oncogene) | 35 (0.8) | 303.3 |
| 28 | Etoposide 100 mg inj | L01CB01 | 1219 (27.2) | High | Etoposide (Pfizer) | 714 (15.9) | 64.8 | Lymphoside (CCL) | 505 (11.3) | 44.9 |
| 29 | Paclitaxel 260 mg inf | L01CD01 | 71 (1.6) | Low | Intaxel (Atco) | 55 (1.2) | 313.5 | Pacliixil (A.J. Mirza) | 16 (0.4) | 313.5 |
| 30 | Docetaxel 80 mg inj | L01CD02 | 18 (0.4) | Low | Taxotere (Sanofi aventis) | 6 (0.1) | 688.6 | Docekebir (Oncogene) | 12 (0.3) | 674.1 |
| 31 | Cabazitaxel | L01CD04 | 6 (0.1) | Low | Jevtana (Sanofi aventis) | 6 (0.1) | 3085.5 | NA | NA | NA |
| (vi) Other antineoplastic agents (31%, n=3007) |
| 32 | Cisplatin 50 mg inj | L01XA01 | 2276 (50.8) | High | Cisplasol (Pfizer) | 1584 (35.3) | 28.1 | Platosin (Pharmachemie) | 692 (15.4) | 15.9 |
| 33 | Carboplatin 150 mg inj | L01XA02 | 206 (4.6) | Low | Carpsol (Pfizer) | 114 (2.5) | 60.5 | Carboplatin (Atco) | 92 (2.1) | 27.2 |
| 34 | Oxaliplatin 100 mg infusion | L01XA03 | 288 (6.4) | Medium | Oxitan (Atco) | 202 (4.5) | 543.6 | Eloxatin (Sanofi aventis) | 86 (1.9) | 475.7 |
| (vii) Other immunosuppressants (1.2%, n = 115) |
| 35 | Hydroxyurea 500 mg cap | L01XX05 | 43 (1.0) | Low | Hydra (Medinet) | 22 (0.5) | 10.9 | Hydrine (Al-Habib) | 21 (0.5) | 10.6 |
| 36 | Topotecan | L01XX17 | 13 (0.3) | Low | Hycamtin (GSK) | 2 (0.04) | 2122.5 | Topokebir (Oncogene) | 11 (0.2) | 906 |
| 37 | Irinotecan 100 mg inj | L01XX19 | 181 (4.0) | Low | Campto (Pfizer) | 74 (1.7) | 1209.3 | Irinocan (Pharmedic) | 107 (2.3) | 645.5 |
| (B) Biologics (3.7%, n=374) |
| 40 | Imatinib mesylate 400 mg tab | L01XE01 | 67 (1.5) | Low | Glivec (Novartis) | 67 (1.5) | 1268.4 | NA | NA | NA |
| 41 | Erlotinib | L01XE03 | 7 (0.1) | Low | Tarceva (Roche) | 7 (0.1) | 1514.2 | NA | NA | NA |
| 42 | Sunitinib 50 mg cap | L01XE04 | 67 (1.5) | Low | Sutent (Pfizer) | 67 (1.5) | 3557.3 | NA | NA | NA |
| 43 | Sorafenib 200 mg tab | L01XE05 | 43 (1.0) | Low | Nexavar (Bayer) | 43 (1.0) | 4218.3 | NA | NA | NA |
| 44 | Lapatinib 250 mg tab | L01XE07 | 43 (1.0) | Low | Tykerb (GSK) | 43 (1.0) | 1826.9 | NA | NA | NA |
| 45 | Nilotinib 200 mg cap | L01XE08 | 43 (1.0) | Low | Tasigna (Novartis) | 43 (1.0) | 4131.4 | NA | NA | NA |
| 46 | Pazopanib 400 mg tab | L01XE11 | 67 (1.5) | Low | Votrient (GSK) | 67 (1.5) | 1600.6 | NA | NA | NA |

Table 2 Continued
The high prices of OBs and unavailability of LPGs for non-biologics in general and biologic drugs in particular are the global issues in the treatment of cancer. The present study aimed to highlight this ongoing scenario of cancer therapy.

**Availability of OB and LPGs**

The accessibility of bioequivalent LPGs is crucial for increasing survival rates of patients with cancer. These agents must be made available in all public and private healthcare settings, but unfortunately they are unavailable in many LMICs. Similarly, the findings of the current study showed that the overall availability of OBs (43.9%) was comparatively higher than the LPGs (21.3%) in both sectors. Most of the OBs are patent protected, and the products of the multinational pharmaceutical companies (MPCs). These MPCs spend a huge amount of money on several promotional techniques in order to compete with the local pharmaceutical companies (LPCs) (eg, conducting conferences, continuing medical education for prescribers, awareness campaigns for the patients and providing the opportunities to the physicians of attending foreign conferences), but financial constraints forbid the LPCs for adopting those strategies. In this way, MPCs successfully promote their products and prescribers are compelled to prescribe these medicines. Hence, the lowest profit margin and collaborative working of LPCs and MPCs are needed for making anticancer drugs available and affordable to the financially constrained patients.

In LMICs, the availability of medicines in the healthcare settings is considerably influenced by the cost. This study revealed that the availability of these anticancer medicines was high in the private sector (62.5% for OBs and 15.6% for LPGs) compared with the government healthcare settings (25.1% for OBs and 8.8% for LPGs). In Pakistan, the provision of health facilities in private sectors is far better than the government sectors. Due to financial crises, the government of Pakistan is unable to maintain good infrastructure of the public healthcare settings. The government hospitals often face the issue of unavailability or shortage of medicines. This is because the government procures medicines once/twice in a year mainly through the bidding system. On the other hand, private sector is not regulated by the government bodies and prime focus of the private sector is to capture the patient's attention. Moreover, only the patients with a strong economic background choose private sectors for the diagnosis and treatment of their illness. Therefore, best quality of health facilities are provided to the patients in private healthcare settings.

Similarly, a country-level survey conducted by the WHO in 2001 revealed that the availability of anticancer medicines was very low (43%) in the South-East Asia, compared with its availability in European region (91%). The unavailability of medicines in the public sector leads to untoward outcomes for the patients and disease progression. The unavailability or shortage of anticancer medicines in the USA compels...
Table 3  Availability of anticancer medicines in public and private sectors in Punjab, Pakistan

| Sr. No | Medicine and dose | Public hospitals (n = 18) | Private hospitals (n = 4) | Private pharmacies (n = 44) | All (n = 66) |
|--------|-------------------|---------------------------|--------------------------|-----------------------------|--------------|
|        | OB LPG            | OB LPG                    | OB LPG                   | OB LPG                      | OB LPG       |
| (A) Non-biologics |                  |                           |                          |                             |              |
| (i) Alkylating agent |          |                           |                          |                             |              |
| 1      | Cyclophosphamide 500 mg inj | 15 (83.3) | 3 (16.7) | 4 (100) | 0 (0.0) | 41 (93.2) | 9 (20.5) | 60 (91.0) | 12 (18.2) |
| 2      | Ifosfamide 1 g inj | 5 (27.8) | 2 (11.1) | 2 (50.0) | 0 (0.0) | 19 (42.3) | 21 (47.7) | 26 (39.4) | 21 (31.8) |
| 3      | Temozolomide      | 0 (0.0) | 0 (0.0) | 1 (25.0) | 0 (0.0) | 9 (20.5) | 0 (0.0) | 10 (15.2) | 0 (0.0)   |
| 4      | Dacarbazine 200 mg inj | 4 (22.2) | 1 (5.6) | 2 (50.0) | 1 (25.0) | 27 (61.4) | 13 (29.5) | 33 (50.0) | 15 (22.7) |
| Total percentage |            | 33.3 | 8.3 | 56.3 | 6.3 | 54.6 | 24.4 | 48.9 | 18.2 |
| (ii) Hormone antagonist |          |                           |                          |                             |              |
| 5      | Tamoxifen 20 mg tab | 15 (83.3) | 2 (11.1) | 4 (100) | 2 (50.0) | 44 (100) | 16 (36.4) | 63 (95.5) | 20 (30.3) |
| 6      | Bicalutamide 50 mg tab | 0 (0.0) | 0 (0.0) | 1 (25.0) | 0 (0.0) | 3 (6.8) | 1 (2.3) | 4 (6.1) | 1 (1.5)   |
| 7      | Anastrozole 1 mg tab | 0 (0.0) | 0 (0.0) | 1 (25.0) | 0 (0.0) | 4 (9.1) | 2 (4.5) | 5 (7.6) | 2 (3.0)   |
| 8      | Letrozole 2.5 mg tab | 0 (0.0) | 0 (0.0) | 2 (50.0) | 0 (0.0) | 16 (36.4) | 8 (18.2) | 18 (27.2) | 8 (12.1) |
| 9      | Cyproterone acetate 50 mg tab | 7 (38.9) | NA | 4 (100) | NA | 39 (88.6) | NA | 50 (76.0) | NA |
| Total percentage |            | 24.4 | 2.8 | 60.0 | 12.5 | 48.2 | 15.3 | 42.4 | 11.7 |
| (iii) Antimetabolite |         |                           |                          |                             |              |
| 10     | Pemetrexed        | 0 (0.0) | 0 (0.0) | 2 (50.0) | 0 (0.0) | 9 (20.5) | 0 (0.0) | 11 (16.7) | 0          |
| 11     | Mercaptopurine 50 mg tab | 13 (72.2) | 3 (16.7) | 4 (100) | 0 (0.0) | 41 (93.2) | 11 (25.0) | 58 (88.0) | 14 (21.2) |
| 12     | Fludarabine phosphate 50 mg inj | 0 (0.0) | 0 (0.0) | 4 (100) | 1 (25.0) | 11 (25.0) | 4 (9.1) | 15 (23.0) | 5 (7.6)   |
| 13     | Cytarabine 100 mg inj | 3 (16.7) | 0 (0.0) | 3 (75.0) | 1 (25.0) | 34 (77.3) | 7 (15.9) | 40 (61.0) | 8 (12.1) |
| 14     | Fluorouracil 500 mg inj | 16 (88.9) | 0 (0.0) | 4 (100) | 2 (50.0) | 44 (100) | 19 (43.2) | 64 (97.0) | 21 (31.8) |
| 15     | Gemcitabine 1 g inj | 5 (27.8) | 11 (61.1) | 4 (100) | 2 (50.0) | 31 (70.5) | 41 (93.2) | 40 (61.0) | 54 (81.8) |
| 16     | Capecitabine 500 mg tab | 4 (22.2) | NA | 4 (100) | NA | 21 (47.7) | NA | 29 (44.0) | NA |
| Total percentage |            | 32.5 | 12.9 | 89.3 | 25.0 | 62.0 | 31.1 | 55.6 | 25.8 |
| (iv) Cytotoxic antibiotics |       |                           |                          |                             |              |
| 17     | Dactinomycin 0.5 mg inj | 8 (44.4) | 2 (11.1) | 3 (75.0) | 1 (25.0) | 42 (95.5) | 31 (70.5) | 53 (80.3) | 34 (51.5) |
| 18     | Doxorubicin 50 mg inj | 14 (77.8) | 4 (22.2) | 4 (100) | 2 (50.0) | 44 (100) | 31 (70.5) | 62 (94.0) | 37 (56.1) |
| 19     | Daunomycin 20 mg inj | 2 (11.1) | 0 (0.0) | 1 (25.0) | 1 (25.0) | 16 (36.4) | 11 (25.0) | 19 (29.0) | 12 (18.2) |
| 20     | Epirubicin 50 mg inj | 2 (11.1) | 3 (16.7) | 4 (100) | 1 (25.0) | 14 (31.8) | 9 (20.5) | 20 (30.3) | 13 (19.7) |
| 21     | Idarubicin        | 0 (0.0) | 0 (0.0) | 2 (50.0) | 0 (0.0) | 7 (15.9) | 0 (0.0) | 9 (13.6) | 0          |
| 22     | Mitoxantrone 20 mg inj | 0 (0.0) | NA | 3 (75.0) | NA | 18 (40.9) | NA | 21 (32.0) | NA |
| 23     | Bleomycin 15 mg inj | 10 (55.6) | 8 (44.4) | 4 (100) | 2 (50.0) | 41 (93.2) | 27 (61.4) | 55 (83.3) | 37 (56.1) |
| 24     | Mitomycin 10 mg inj | 2 (11.1) | 0 (0.0) | 2 (50.0) | 1 (25.0) | 31 (70.5) | 12 (27.3) | 35 (53.0) | 13 (19.7) |

Continued
| Sr. No | Medicine and dose | Public hospitals (n = 18) | Private hospitals (n = 4) | Private pharmacies (n = 44) | All (n = 66) |
|--------|-------------------|--------------------------|--------------------------|-----------------------------|-------------|
|        |                   | OB | LPG | OB | LPG | OB | LPG | OB | LPG |
| (v) Plant alkaloids | | | | | | | | | |
| 25     | Vinblastine 10 mg inj | 9 (50.0) | 3 (16.7) | 4 (100) | 0 (0.0) | 31 (70.5) | 19 (43.2) | 44 (67.0) | 34 (51.5) |
| 26     | Vincristine 2 mg inj  | 11 (61.1) | 2 (11.1) | 3 (75.0) | 0 (0.0) | 33 (75.0) | 23 (52.3) | 47 (71.2) | 25 (37.9) |
| 27     | Vinorelbine 50 mg inj | 0 (0.0) | 0 (0.0) | 2 (50.0) | 2 (50.0) | 21 (47.7) | 11 (25.0) | 23 (35.0) | 13 (19.7) |
| 28     | Etoposide 100 mg inj | 15 (83.3) | 0 (0.0) | 4 (100) | 0 (0.0) | 44 (100) | 13 (29.5) | 63 (95.4) | 13 (19.7) |
| 29     | Paclitaxel 260 mg inj | 11 (61.1) | 4 (22.2) | 3 (75.0) | 1 (25.0) | 44 (100) | 23 (52.3) | 58 (88.0) | 28 (42.4) |
| 30     | Docetaxel 80 mg inj  | 7 (38.9) | 0 (0.0) | 3 (75.0) | 0 (0.0) | 33 (75.0) | 7 (15.9) | 43 (65.1) | 7 (10.6) |
| 31     | Cabazitaxel         | 0 (0.0) | 0 (0.0) | 1 (25.0) | 0 (0.0) | 4 (9.1) | 0 (0.0) | 5 (7.6) | 0 (0.0) |
| Total  |                   | 42.1 | 7.1 | 71.4 | 10.7 | 68.2 | 31.2 | 61.3 | 25.9 |
| (vi) Other antineoplastic agents | | | | | | | | | |
| Platinum compounds | | | | | | | | | |
| 32     | Cisplatin 50 mg inj | 8 (44.4) | 9 (50.0) | 3 (75.0) | 0 (0.0) | 43 (97.7) | 11 (25.0) | 54 (82.0) | 20 (30.3) |
| 33     | Carboplatin 150 mg inj | 13 (72.2) | 5 (27.8) | 4 (100) | 1 (25.0) | 33 (75.0) | 29 (65.9) | 50 (76.0) | 35 (53.0) |
| 34     | Oxaplatin 100 mg inj | 1 (5.6) | 0 (0.0) | 2 (50.0) | 2 (50.0) | 21 (47.7) | 11 (25.0) | 24 (36.4) | 13 (19.7) |
| Total  |                   | 40.7 | 25.9 | 75.0 | 25.0 | 73.5 | 38.6 | 64.7 | 34.3 |
| Others | | | | | | | | | |
| 35     | Hydroxyurea 500 mg cap | 7 (38.9) | 0 (0.0) | 3 (75.0) | 0 (0.0) | 23 (52.3) | 11 (25.0) | 33 (50.0) | 11 (16.7) |
| 36     | Topotecan           | 0 (0.0) | 0 (0.0) | 1 (25.0) | 1 (25.0) | 4 (9.1) | 5 (11.4) | 5 (7.6) | 5 (7.6) |
| 37     | Irinotecan 100 mg inj | 0 (0.0) | 0 (0.0) | 2 (50.0) | 0 (0.0) | 11 (25.0) | 10 (22.7) | 13 (20.0) | 10 (15.2) |
| Total  |                   | 12.9 | 0.0 | 50.0 | 8.3 | 28.8 | 19.7 | 25.8 | 13.1 |
| (vii) Other immunosuppressants | | | | | | | | | |
| 38     | Thalidomide 100 mg cap | 4 (22.2) | NA | 4 (100) | NA | 25 (56.8) | NA | 33 (50.0) | NA |
| 39     | Methotrexate 10 mg tab | 15 (83.3) | 1 (5.6) | 4 (100) | 1 (25.0) | 44 (100) | 19 (43.2) | 63 (95.4) | 21 (31.8) |
| Total  |                   | 52.8 | 2.8 | 100 | 12.5 | 78.4 | 21.6 | 72.7 | 15.9 |
| Total percentage (non-biologics) | | | | | | | | | |
| 32.2 | 10.0 | 71.8 | 17.8 | 59.4 | 30.2 | 52.8 | 24.3 |
| (B) Biologics | | | | | | | | | |
| Protein kinase inhibitors | | | | | | | | | |
| 40     | Imatinib mesylate 400 mg tab | 0 (0.0) | NA | 3 (75.0) | NA | 15 (34.1) | NA | 18 (27.3) | NA |
| 41     | Erlotinib           | 0 (0.0) | 0 (0.0) | 2 (50.0) | 0 (0.0) | 5 (11.4) | 0 (0.0) | 7 (10.6) | 0 |
| 42     | Sunitinib 50 mg cap | 0 (0.0) | NA | 0 (0.0) | NA | 3 (6.8) | NA | 3 (4.5) | NA |
| 43     | Sorafenib 200 mg tab | 0 (0.0) | NA | 1 (25.0) | NA | 5 (11.4) | NA | 6 (9.1) | NA |
| 44     | Lapatinib 250 mg tab | 0 (0.0) | NA | 2 (50.0) | NA | 13 (29.6) | NA | 15 (23.0) | NA |
the hospitals to purchase costly substitute with the annual expense of US$200 million–US$216 million.32 However, a restraint healthcare sector such as government hospitals of an economically developing country like Pakistan finds it very difficult to bear such expenses. The responsibility lies on the government to provide adequate funds and pay attention towards the development of new healthcare projects.

**Availability of biologics versus non-biologics anticancer medicines**

Unlike the non-biologics such as platinum compounds, alkylating agents, plant alkaloids, antimetabolites and hormone antagonist, biologics were less readily available in both sectors. Moreover, none of the biosimilar or generic version was available for any of the selected biologics (table 4) because of prolonged patent period and data exclusivity. According to the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement, Pakistan has a right to include in its patent legislation a provision of manufacturing LPGs without the requisition of any consent from the patent holder since Pakistan is a member of the World Trade Organization. Many developed countries have imposed data exclusivity on low/middle-income countries including Pakistan since regulatory approval depends on the bioequivalence studies which in turn depends on originator’s data.33 Furthermore, the unavailability of facilities (instruments, methods/techniques, skilled personnel) for the manufacturing process hinders the availability of biosimilar products. Though no country can ensure the availability of all biologic anticancer medicines but certain countries such as Japan and Spain have made nearly half of the biologics available for patients with cancer.34 Currently, India is manufacturing many new entities for cancer treatment, but their import is prohibited in Pakistan because of several political issues. Internationally, the focus is being given on the research of biological medicines for cancer treatment because these agents are more effective compared with the pharmaceutical moieties. However, in Pakistan, the government shows reluctance towards the availability of biosimilar products. It can be possibly attributed to the fact that these agents need expensive testing like clinical trials to ensure their similarity with the biologics. Thus, safety guidelines of the WHO must be implicated on national level for the availability of biosimilar products. Otherwise, non-comparable biosimilar products can be deleterious for the patients. Hence, it is recommended that patent periods must be limited. Also, government should add TRIPS flexibility in its patent legislation. In this way, LPCs can have legal rights to manufacture LPGs.

In LMICs like Pakistan, the retail prices are the major deterrent to access when compared with the cost at the supplier level.35 Owing to this reason, the availability of non-biologics (OBs=52.8%, LPGs=24.3%) in the current study was found to be less than 100%. In Pakistan, anticancer medicines do not enjoy tax-free status, so the high taxation associated with these life-saving medicines is a huge burden for the cancer sufferers. All the national and international organisations such as the WHO, HAI, The United States Agency for International Development, United Nations Organization and Drug Regulatory Authority of Pakistan must provide adequate funding so that tax-free anticancer medicines can be made available to the local masses.

### Table 3

Continued

| Sr. No | Medicine and dose | Public hospitals (n = 18) | Private hospitals (n = 4) | Private pharmacies (n = 44) | All (n = 66) |
|--------|-------------------|--------------------------|---------------------------|-----------------------------|-------------|
|        | OB LPG            | OB LPG                   | OB LPG                    | OB LPG                      | OB LPG      |
| 45     | 0 (0.0) | 0 (0.0) | 19 (43.2) | 3 (75.0) | 3 (6.8) | 3 (4.6) | 22 (33.3) | 14.9 |
| 46     | 0 (0.0) | 0 (0.0) | 1 (25.0) | 0 (0.0) |
| 47     | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Total  | 0.0    | 37.5  | 0.0     | 19.0  | 0.0     | 0.0     | 14.9    | 0.0  |
| Monoclonal antibodies |
| 48     | 0 (0.0) | 0 (0.0) | 5 (11.4) | 1 (25.0) | 0 (0.0) | 2 (4.6) | 6 (9.1) | 0 (0.0) |
| 49     | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 50     | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Total  | 0.0    | 8.3   | 0.0     | 6.8   | 0.0     | 5.1     | 12.3    | 0.0  |
| Total percentage (biologics) | 25.1 | 8.8 | 62.5 | 15.6 | 49.8 | 26.4 | 43.9 | 21.3 |

cap, capsule; inj, injection; LPG, lowest price generic; NA, not available; OB, originator brand; tab, tablet.
## Table 4
Affordability of anticancer medicines by high-income, middle-income and low-income class patients in Punjab, Pakistan

| Sr. No. | Medicine and dose | OB Overall | Overall OB | LPG Overall | Overall both (OB+LPG) |
|---------|-------------------|------------|-----------|-------------|----------------------|
|         |                   | High | Middle | Low | OB | High | Middle | Low | LPG | High | Middle | Low | (OB+LPG) |
| (A) Non-biologics |  |  |  |  |  |  |  |  |  |  |  |  |
| (i) Alkylating agent |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | Cyclophosphamide 500 mg inj | 100 | 65.5 | 28.0 | 70.5 | 100 | 95.9 | 57 | 86.6 | 77.0 |
| 2 | Ifosfamide 1 g inj | 62.9 | 29.5 | 9.1 | 42.3 | 62.9 | 29.2 | 8.8 | 33.5 | 38.8 |
| 3 | Temozolomide | 2.6 | 1.9 | 0.4 | 1.6 | NA | NA | NA | NA | 1.6 |
| 4 | Dacarbazine 200 mg inj | 100 | 77.8 | 53.6 | 78.3 | 100 | 100 | 67.9 | 90 | 83.4 |
| Total |  | 66.4 | 43.7 | 22.8 | 48.2 | 87.6 | 75.0 | 44.7 | 70.0 | 50.2 |
| (ii) Hormone antagonist |  |  |  |  |  |  |  |  |  |  |  |  |
| 5 | Tamoxifen 20 mg tab | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 6 | Bicalutamide 50 mg tab | 100 | 28.2 | 12.4 | 48.9 | 100 | 100 | 73.8 | 93.3 | 66.4 |
| 7 | Anastrozole 1 mg tab | 100 | 50.1 | 18.3 | 71.5 | 100 | 68.3 | 20.6 | 63.2 | 68.2 |
| 8 | Letrozole 2.5 mg tab | 86.5 | 40.7 | 12.6 | 58.3 | 100 | 68.7 | 20.7 | 63.3 | 60.3 |
| 9 | Cyproterone acetate 50 mg tab | 100 | 99.5 | 43.8 | 84.5 | NA | NA | NA | NA | 84.5 |
| Total |  | 97.3 | 63.7 | 37.4 | 72.6 | 100 | 84.3 | 53.8 | 79.9 | 75.9 |
| (iii) Antimetabolite |  |  |  |  |  |  |  |  |  |  |  |  |
| 10 | Pemtrexed | 2.9 | 1.8 | 0.6 | 1.8 | NA | NA | NA | NA | 1.8 |
| 11 | Mercaptopurine 50 mg tab | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 12 | Fludarabine phosphate 50 mg inj | 30.1 | 8.2 | 2.8 | 15.9 | 40.3 | 11.1 | 5.1 | 2.7 | 17.8 |
| 13 | Cytarabine 100 mg inj | 100 | 69.9 | 92.5 | 100 | 100 | 100 | 100 | 94.7 |
| 14 | Flouorouracil 500 mg inj | 100 | 60.9 | 90.6 | 100 | 100 | 100 | 100 | 100 | 94.4 |
| 15 | Gemcitabine 1 g inj | 21.3 | 9.7 | 3.5 | 13.2 | 32.4 | 13.5 | 5.2 | 18.1 | 15.1 |
| 16 | Capecitabine 500 mg tab | 61.9 | 25.0 | 8.1 | 35.5 | NA | NA | NA | NA | 35.5 |
| Total |  | 45.2 | 49.2 | 35.1 | 49.9 | 74.5 | 64.9 | 62.1 | 64.2 | 51.3 |
| (iv) Cytotoxic antibiotics |  |  |  |  |  |  |  |  |  |  |  |  |
| 17 | Dactinomycin 0.5 mg inj | 100 | 42.6 | 14.7 | 66.1 | 100 | 51.8 | 17.8 | 56.4 | 62.3 |
| 18 | Doxorubicin 50 mg inj | 100 | 62.5 | 27.8 | 68.7 | 100 | 93.5 | 39.5 | 80.3 | 73.0 |
| 19 | Daunomycin 20 mg inj | 100 | 50.3 | 15.7 | 58.1 | 100 | 100 | 43.3 | 85.6 | 69.0 |
| 20 | Epirubicin 50 mg inj | 75.3 | 28.6 | 9.0 | 44.2 | 96.4 | 38.1 | 19.1 | 55.3 | 48.6 |
| 21 | Idarubicin | 4.8 | 3.2 | 0.3 | 2.8 | NA | NA | NA | NA | 2.8 |
| 22 | Mitoxantrone 20 mg inj | 100 | 100 | 52.5 | 90.1 | NA | NA | NA | NA | 90.1 |
| 23 | Bleomycin 15 mg inj | 68.3 | 18.1 | 6.5 | 27.8 | 78.8 | 46.6 | 15.4 | 46.9 | 36.0 |
| 24 | Mitomycin 10 mg inj | 100 | 100 | 48.5 | 89.2 | 100 | 100 | 100 | 100 | 93.5 |
| Total |  | 81.1 | 50.7 | 21.9 | 55.9 | 95.9 | 71.7 | 39.2 | 70.8 | 59.4 |
| (v) Plant alkaloids |  |  |  |  |  |  |  |  |  |  |  |  |
| 25 |Vinblastine 10 mg inj | 100 | 43.2 | 15.6 | 50.5 | 100 | 100 | 43.9 | 81.3 | 63.7 |
| 26 | Vincristine 2 mg inj | 100 | 100 | 85.2 | 96.3 | 100 | 100 | 99.4 | 99.8 | 97.6 |
| 27 | Vinorelbine 50 mg inj | 100 | 8.7 | 4.8 | 54.6 | 100 | 15.1 | 5.1 | 39.2 | 48.5 |

Continued
### Table 4  Continued

| Sr. No. | Medicine and dose | OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-------------------|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 28      | Etoposide 100 mg inj | 100     | 77.4      | 31.0   | 74.6       | 100      | 92.4       | 43.9    | 82.1        | 77.6                 |
| 29      | Paclitaxel 260 mg inf | 23.9    | 8.5       | 4.6    | 15.6       | 23.9     | 14.6       | 5.0     | 14.5        | 15.1                 |
| 30      | Docetaxel 80 mg inj | 31.8    | 5.5       | 3.2    | 15.1       | NP       | NP         | NP      | NP          | 15.1                 |
| 31      | Cabazitaxel         | 100     | 36.7      | 28.4   | 55.0       | NA       | NA         | NA      | NA          | 55.0                 |
| Total   |                    | 79.4    | 40.0      | 24.7   | 51.7       | 84.8     | 64.4       | 39.5    | 63.4        | 53.2                 |

(vi) Other antineoplastic agents

#### Platinum compounds

| Sr. No. | Medicine and dose | OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-------------------|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 32      | Cisplatin 50 mg inj | 100     | 100       | 60     | 91.6       | 100      | 100        | 97.5    | 99.3        | 94.4                 |
| 33      | Carboplatin 150 mg inj | 100 | 93.1     | 32.7   | 79.3       | 100      | 100        | 77.1    | 93.6        | 85.0                 |
| 34      | Oxalplatin 100 mg inf | 14.5    | 5.8       | 2.0    | 8.2        | 18.0     | 6.6         | 3.5     | 10.3        | 9.1                  |
| Total   |                    | 71.5    | 66.3      | 31.6   | 59.7       | 72.7     | 68.9        | 59.4    | 67.7        | 62.8                 |

Others

| Sr. No. | Medicine and dose | OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-------------------|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 35      | Hydroxyurea 500 mg cap | 100     | 100       | 100    | 100        | NP       | NP         | NP      | NP          | 100                  |
| 36      | Topotecan         | 3.2     | 2.4       | 1.9    | 2.5        | 20.1     | 18.7       | 6.2     | 15.6        | 9.1                  |
| 37      | Irinotecan 100 mg inj | 6.7     | 2.2       | 1.0    | 3.8        | 11.6     | 4.4         | 2.1     | 6.5         | 4.9                  |
| Total   |                    | 36.6    | 34.9      | 34.3   | 35.4       | 15.9     | 11.6        | 4.2     | 11.1        | 38.0                 |

(vii) Other immunosuppressants

| Sr. No. | Medicine and dose | OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-------------------|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 38      | Thalidomide 100 mg cap | 100     | 67.7      | 24.3   | 75.1       | NA       | NA         | NA      | NA          | 75.1                 |
| 39      | Methotrexate 10 mg tab | 100     | 100       | 100    | 100        | 100      | 100        | 100     | 100         | 100                  |
| Total   |                    | 100     | 83.9      | 62.2   | 87.6       | 100      | 100        | 100     | 100         | 87.6                 |

Total non-biologics

| OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 74.3    | 51.1      | 31.6   | 56.1       | 82.2     | 67.9       | 47.5    | 66.1        | 58.1                 |

(B) Biologics

### Protein kinase inhibitors

| Sr. No. | Medicine and dose | OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-------------------|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 40      | Imatinib mesylate 400 mg tab | 7.2     | 2.4       | 0.8    | 3.6        | NA       | NA         | NA      | NA          | 3.6                  |
| 41      | Erlotinib         | 2.1     | 1.4       | 0.7    | 1.4        | NA       | NA         | NA      | NA          | 1.4                  |
| 42      | Sunitinib 50 mg cap | 6.7     | 1.6       | 0.6    | 3.1        | NA       | NA         | NA      | NA          | 3.1                  |
| 43      | Sorafenib 200 mg tab | 6.3     | 3.2       | 1.1    | 4.3        | NA       | NA         | NA      | NA          | 4.3                  |
| 44      | Lapatinib 250 mg tab | 8.0     | 3.0       | 1.0    | 5.1        | NA       | NA         | NA      | NA          | 5.1                  |
| 45      | Nilotinib 200 mg cap | 2.2     | 0.9       | 0.3    | 1.4        | NA       | NA         | NA      | NA          | 1.4                  |
| 46      | Pazopanib 400 mg tab | 14.8    | 3.5       | 1.4    | 6.8        | NA       | NA         | NA      | NA          | 6.8                  |
| 47      | Ruxolitinib       | 5.1     | 3.1       | 2.6    | 3.6        | NA       | NA         | NA      | NA          | 3.6                  |
| Total   |                    | 6.6     | 2.4       | 1.1    | 3.7        | NA       | NA         | NA      | NA          | 3.7                  |

Monoclonal antibodies

| Sr. No. | Medicine and dose | OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-------------------|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 48      | Rituximab         | 3.9     | 2.3       | 1.1    | 2.4        | NA       | NA         | NA      | NA          | 2.4                  |
| 49      | Trastuzumab       | 2.3     | 1.2       | 0.5    | 1.3        | NA       | NA         | NA      | NA          | 1.3                  |
| 50      | Cetuximab         | 5.4     | 2.2       | 1.5    | 3.0        | NA       | NA         | NA      | NA          | 3.0                  |
| Total   |                    | 3.9     | 1.9       | 1.0    | 2.2        | NA       | NA         | NA      | NA          | 2.2                  |

Total biologics

| OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 5.8     | 2.3       | 1.1    | 3.3        | NA       | NA         | NA      | NA          | 3.3                  |

### Overall total (biologics+non-biologics)

| OB High | OB Middle | OB Low | Overall OB | LPG High | LPG Middle | LPG Low | Overall LPG | Overall both (OB+LPG) |
|---------|-----------|--------|------------|----------|------------|---------|-------------|----------------------|
| 59.2    | 40.4      | 24.1   | 44.2       | 82.2     | 67.9       | 47.5    | 66.1        | 46.0                 |

cap, capsule; inj, injection; LPG, lowest price generic; NA, not available; NP, not prescribed; OB, originator brand; tab, tablet.
Affordability of anticancer medicines of OB and LPGs

The elevated prices of anticancer medicines have made the treatment unaffordable for patients. In Pakistan, the proliferation of OBs has economically burdened the local masses, especially the cancer sufferers. Our findings show that the LPGs (66.1%) are more affordable than the OBs (44.2%). These lifesaving drugs must be affordable for all income classes but our findings depict the greater affordability (59.2%) of OBs for high-income patients, less (40.4%) for middle-income patients and least (24.1%) for low-income patients. In this study, the overall affordability for both OBs and LPGs was found to be 46% which makes cancer a catastrophic disease, especially for those patients who live below the poverty line in Pakistan. Unfortunately, the lack of awareness about health insurance has also worsened the situation. Another dilemma of LMICs is that the local masses are unaware of the importance of health insurance. Insurance policies fail to provide benefits or demand substantial copayment. Therefore, in 2014 the Pakistani government took an initiative in the form of the Prime Minister National Health Insurance Program. This programme aimed to cover a large number of cancer sufferers in both government and private sectors. However, this programme cannot cover the entire financially constrained civilians of Pakistan without the cooperation of international organisations. The government of Pakistan should follow the footsteps of developed countries where the equality in terms of affordability is being given to every citizen due to their health insurance policies. Health sector and the bank sector must join hands to spread awareness regarding the beneficial attributes of health insurance schemes.

Affordability of biologic versus non-biologic anticancer medicines

Our findings showed that biologics (3.3%) were less affordable than non-biologics (58.1%). Affordability of biologics in cancer therapy is particularly a huge problem for both high-income countries and LMICs. In 2011, a drug expenditure analysis demonstrated that biologic anticancer medicines accounted for 55% of the health expenditure in the USA. The advent of biologics has improved the survival rate but patients usually show non-compliance and discontinue therapy within 6 months. Previously published literature has declared the high cost as a barrier towards patient’s adherence. This leads to disease progression and treatment resistance.

The findings also demonstrated that non-biologic anticancer medicines (31.6%) were more affordable for low-income patients than biologic medicines (1.1%). As per an estimation made in 2017, 11% of the Pakistani population are living below the poverty line, and a person can earn an average of PKR12000–PKR13000 (US$108.3–US$117.3) per month which amounts to PKR100–433.33 (US$3.6–US$3.9) per day. Their low monthly income serves as the root cause of unaffordability of biologic medicines. In Pakistan, lack of public health insurance policies and out-of-pocket monthly premium of private health insurance policies have compelled people to bear health expense on their own. In high-income countries like the USA where people earn US$3500–US$4000 a month, the average daily cost of biologics is 22 times higher than that of non-biologics. Such high prices cannot be covered by the public health insurance policies, therefore in high-income countries, insurers have to pay 20% of the drug price.

For biologics, the biosimilars or LPGs are not available, and as a consequence prescribers are compelled to prescribe OBs. According to the Patent Ordinance 2000, the life of a patent is prolonged in Pakistan (ie, 20 years). This has forbidden local manufacturers to make inexpensive versions of the biologics. In Pakistan, there is a dearth of clinical trials. Therefore, biologics have to be imported from developed countries. However, in contrast to European countries, the government is less likely to negotiate on price referencing with the MPCs. Thus, there is a dire need to strengthen the research and development area of both pharmaceutical and biopharmaceutical industries in Pakistan.

CONCLUSION

Current study showed that most of the patients with cancer were prescribed non-biologics due to their low price and better affordability. There was fairly high availability of non-biologics compared with biologics. The overall affordability of LPGs was higher compared with OBs for low-income patients irrespective of the fact whether the cancer medicine was biologic or non-biologic. The inequality in terms of affordability is primarily governed by prolonged patent periods of OBs and lack of awareness regarding health insurance schemes. Thus, it is the need of the hour to pay special consideration on ways of improving national health policies or else cancer will continue to ruin patients physically and financially.

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