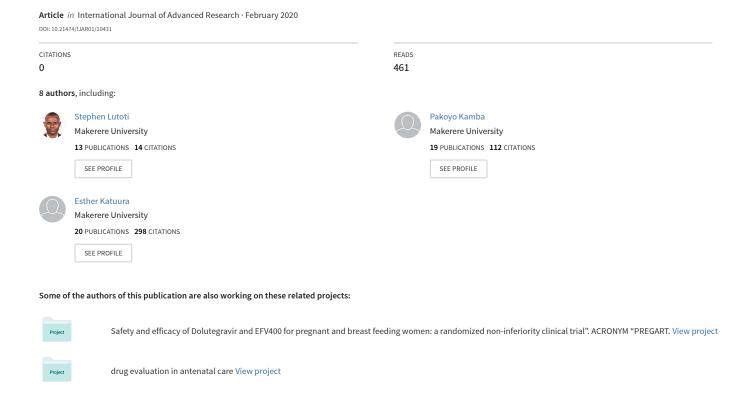# A REVIEW OF BREAST CANCER TREATMENT MODALITIES IN UGANDA : AN APPRAISAL OF THE BREAST CANCER DIAGNOSTIC PROCESS, REGULATORY APPROVAL AND SUPPLY SYSTEM OF STANDARDIZED ANTI-BREAST C…

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RESEARCH ARTICLE

A REVIEW OF BREAST CANCER TREATMENT MODALITIES IN UGANDA : AN APPRAISAL OF THE BREAST CANCER DIAGNOSTIC PROCESS, REGULATORY APPROVAL AND SUPPLY SYSTEM OF STANDARDIZED ANTI-BREAST CANCER MEDICINES

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Abstract

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Breast cancer is the leading cause of cancer death among women and the third incident cancer in the world, contributing 1.7 million of the 17.2 million annual incident cancer cases. For Uganda, breast cancer is the third incident cancer and fourth cause of cancer related deaths. The Uganda cancer treatment guidelines focuses on treatment of five cancers that constitute 60% of the national cancer burden, namely; Kaposi sarcoma, cancer of cervix, prostate cancer, esophageal cancer and breast cancer. We present a review of the treatment modalities of breast cancer based upon Uganda's treatment guidelines as well as documented clinical practices. Diagnosis of breast cancer is delayed in most patients and based on clinical evaluation of risk factors, clinical manifestations and laboratory investigations. Staging is based on The American Joint Committee on Cancer TNM system. Surgery, radiotherapy and chemotherapy are the recommended treatment options administered singly or in combination with each other depending on the stage of breast cancer at the time of diagnosis. We found 21 standard treatment regimens based on 17 drug molecules have been recommended for various breast cancers. Seven of these molecules are among 13 other cytotoxic drugs approved by WHO as essential anti-breast cancer medicines. 39 brands of these drug molecules were found registered by the National drug Authority in Uganda as of 23rdAugust 2018, accounting for 0.01% of all the registered drugs for human use in Uganda.

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Introduction:-

Breast cancer is the leading cause of cancer death among women and third incident cancer in the world, contributing 1.7 million of the 17.2 million incident cancer cases in 131 countries[1]. At least 99% of breast cancer cases are women in 112 countries; with 1 in 20 women developing breast cancer over a lifetime[1], [2].

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Based on the number of incident cases for both sexes, breast cancer is the first incident cancer overall in 15 countries, second in 13 countries, third in 15 countries, fourth in 5 countries, fifth in 8 countries, sixth in 2 countries and seventh incident cancer in 1 country[3]. Based on cancer related mortality rates, breast cancer is ranked first in 5 countries, second in 4 countries, third in 11 countries, fourth cancer in 14 countries, fifth in 6 countries, sixth in 6 countries, seventh in 3 countries, eighth in 3 countries and tenth in 1 country[3].

The burden of breast cancer in Uganda is the highest compared to other countries within the Eastern Sub-Saharan African region, being reported as the third incident cancer and fourth leading cause of death due to cancers in Uganda[4]. This is in comparison to its ranking as a fifth incident cancer in Tanzania, Kenya and Mozambique but eighth, sixth and sixth leading cause of death due to cancers in those countries respectively. For Ethiopia, breast cancer has been ranked as fourth incident cancer and sixth cause of death due to cancer[3].

In response to the cancer burden, Uganda has invested in cancer research, training and clinical care. The UCI-Fred Hutch Cancer Centre has significantly increased patient access to cancer diagnosis and treatment while furthering the study of cancers in Uganda, particularly those that are infection-related [4],[5], [6]. This is a review of the various treatment modalities of breast cancer based upon Uganda's Cancer treatment guidelines as well as documented clinical practices and traditional methods of managing breast cancer using herbal medicines.

Risk factors, Classification and Clinical staging of Breast cancer:
Risk factors of Breast cancer:
A risk factor is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury[7]. The risk factors for breast cancer include gender, age, genetic mutations, family history of breast cancer, personal history of breast cancer, race, ethnicity, dense breast tissue, certain begnin breast conditions, lobular carcinoma in situ, menstrual periods, previous chest radiation, diethlystilbesterol, weight, diet, exercise, alcohol consumption, stress and anxiety [3],[2],[8]. Also reported are un proven risk factors like antiperspirants, underwear, bras, induced abortion, night work and antibiotics[8].

Whereas the most common cause of hereditary breast cancer accounting for 5-10% of breast cancer cases is an inherited mutation in the BRCA1 and BRCA2 genes, the presence of these gene mutations is un known in the Ugandan population[1],[8].While the lifetime risk of breast cancer occurring more often in younger women and affecting both breasts is as high as 80% for BRCA1 mutations, the breast cancer risk associated with BRCA2 mutations the risk is around 45% and sadly women with BRCA1 and BRCA2 inherited mutations also have an increased risk for developing other cancers, particularly ovarian cancer[1].

Though much rarer and often do not increase the risk of breast cancer as much as the BRCA genes, there are other gene mutations that can lead to inherited breast cancers and they include mutations in the ATM gene, TP53, CHEK2, PTEN, CDH1, STK11 and PALB2 genes[1].

Classification of Breast cancer:
Breast cancer classification has been the focus of numerous worldwide efforts, analyzing the molecular basis of breast cancer subtypes and aiming to associate them with clinical outcome and improve the current diagnostic routine[8]. Different studies have categorized breast cancer into different groups based on the status of three important receptors namely; estrogen receptor (ER), progesterone receptor (PR), and human epithelial receptor 2 (HER2)[9],[10]. These can be further classified into luminal A, luminal B, HER2 positive, and triple negative subtypes, with triple negative cells being further divided into A and B to capture its heterogeneity and provide an easy link to the widely used names, namely , basal A and B[11],[10].

Xiaofeng et al (2017) have documented the molecular features and corresponding tumor subtype each cell line represents to facilitate breast cancer modeling using appropriate cell lines. They have categorized 84 breast cancer cell lines into luminal A (LA), luminal B (LB), HER2 positive (H), Triple negative A (TNA) and Triple negative B (TNB), according to literature available subtyping suggestions or derived information from the original article where they are established [10].

Staging of breast cancer in Uganda:
The cancer's stage is one of the most important factors in determining prognosis and treatment options. Staging is the process of finding out how widespread a cancer is when it is diagnosed[1]. Uganda has adopted the most

common system used to describe the stages of breast cancer called the American Joint Committee on Cancer (AJCC) TNM system[8]. The stage of a breast cancer can be based either on the results of physical exam, biopsy, and imaging tests called the clinical stage, or on the results of these tests plus the results of surgery called the pathologic stage which has been considered to be more accurate than clinical staging, as it allows the health worker to get a firsthand impression of the extent of the cancer[1].

The TNM staging system classifies cancers based on their T, N, and M stages: The letter T followed by a number from 0 to 4 describes the tumor's size and spread to the skin or to the chest wall under the breast. Higher T numbers mean a larger tumor and/or wider spread to tissues near the breast; the letter N followed by a number from 0 to 3 indicates whether the cancer has spread to lymph nodes near the breast and, if so, how many lymph nodes are affected.; the letter M followed by a 0 or 1 indicates whether the cancer has spread to distant organs[1].

Once the T, N, and M categories have been determined, this information is combined in a process called stage grouping. Cancers with similar stages tend to have a similar outlook and are often treated in a similar way. Stage is expressed in Roman numerals from stage I (the least advanced stage) to stage IV (the most advanced stage). Non-invasive cancer is listed as stage 0 [8],[1].

Clinical presentation and Diagnosis of breast cancer:
The main goal of modern healthcare systems is to diagnosis a disease before its outcomes are worse[12]. Breast cancer is being the most affected disease in women requires to be accurately diagnosed at an early stage[13]. If it is diagnosed at an initial stage, there is a better chance of a cure[14].

The most common symptom of breast cancer is a new lump or mass. A painless, hard mass that has irregular edges is more likely to be cancerous, but breast cancers can be tender, soft, or rounded[8]. They can even be painful. For this reason, any new breast mass or lump or breast change should be checked by a health care professional experienced in diagnosing breast diseases[1].

Other possible symptoms of breast cancer include swelling of all or part of a breast (even if no distinct lump is felt), skin irritation or dimpling, breast or nipple pain, Nipple retraction (turning inward) ;redness, scaliness, or thickening of the nipple or breast skin; Nipple discharge other than breast milk[1].

Sometimes a breast cancer can spread to lymph nodes under the arm or around the collar bone and cause a lump or swelling there, even before the original tumor in the breast tissue is large enough to be felt. Swollen lymph nodes should also be reported to your doctor[1].

Clinical evaluation of breast cancer involves exploring several features during history taking and physical exam of a patient with suspected/ confirmed breast cancer which includes gender and age, age at first parity, age at Menarche, and duration of menstrual cycle, Type of contraceptive, and duration of use, Breast symptoms and signs, Co-morbidity (like HIV infection, Diabetes, hypertension and Heart Disease), Family history of breast and/or ovarian cancer among 1st degree relatives, previous BRCA gene test among first degree relatives, Prior irradiation to the chest wall, previous breast biopsy; and history of atypical ductal hyperplasia, alcohol and tobacco use history, performance status using ECOG score, Body Mass Index (BMI), bimanual palpation of the breasts note the tumor size and location ,skin/chest wall changes and asymmetry and fixation to chest wall) and loco-regional lymph nodes (mobility, matted or fixed), complete physical exam [8].

Investigation of breast cancer patients involves carrying out special tests that include radiological tests (before, at and after biopsy), laboratory tests and optional tests[8]. Optional tests include oncogene assays, Brain CT if suspicious CNS symptoms, PET scan indicated for unsuspected nodal spread and distant metastases in selected cases, ECG/ ECHO if treatment with anthracyclines and Trastuzumab is anticipated[8].

A cross-sectional study carried out at the breast unit of Mulago National Referral Hospital over a period of 4 months between January and April 2014 involving 162 patients indicated that 86 % had clinical stage IV disease and 10 % had clinical stage III disease .The first symptoms noticed were a lump 86 % , pain 12 % and 2 % had abnormal discharge. The mean patient delay and median delay were 22.6 and 13 months respectively, with a range of 1–127 months.The majority (89 %) of patients delayed by more than 3 months after noticing symptoms while only 17 (11 %) patients sought attention within 3 months of noticing symptoms of breast cancer [15].

Early detection of breast cancer has been reported to depend on the decisions of patients and their interactions with social and contextual factors, and in Malawi this pathway is complicated by extreme poverty, cultural beliefs and practices, and an overburdened health system[13].

Odongo et al had earlier observed a significant association between patient delay and lack of social support (OR = 7.12, 95 % CI 2.36–21.46, P = 0.001). They noted a significant association between delayed presentation and advanced stage at presentation (OR = 11.18, 95 % CI 2.01–62.13, P = 0.006), while the association between age, religion, marital status, occupation, education level, monthly income and fear of surgery and patient delay were not significant [15].

In a qualitative study by Meacham et al (2016) on exploring stigma as a barrier to cancer service engagement with breast cancer survivors in Kampala-Uganda, all participants described the shock and devastation of receiving a cancer diagnosis that "breast cancer equaled death" and that "tampering" with the breast was taboo[16]. Patients in this study emphasized the severity of public stigma and pervasive negative social reaction to their diagnosis, such as being told by friends and family that they would die. It was noted that women were often shamed for bringing cancer into their families, especially by their in-laws and that such stigma could lead breast cancer patients to be afraid to engage in screening and care[16].

Ensuring providers at primary care facilities are trained on breast cancer symptoms and clinical breast exam may reduce misdiagnoses and speed up referrals for suspected cancers[13]. Additionally, because health system factors such as distance to the facility and transportation costs were common barriers, expanding services at health centers would increase availability and accessibility. Health care delivery improvement at and coordination between district and central hospitals may address logistical delays patients faced between consultations, biopsy sampling, surgery, and chemotherapy. Interventions to improve patient-provider communication are needed. Counseling and support services might help patients navigate the diagnosis process better, increase patient understanding, and improve treatment plan adherence. Finally, future research should explore the role of traditional healers and the potential to engage them to work with the health system to improve early detection and adherence to treatment[13].

A systematic review by Espinac et al revealed marked delays in presentation and diagnosis of breast cancer in Africa and that identification of their drivers was crucial to the development of appropriate control strategies in the continent [17]. Akuoko et al have argued that improving African women's knowledge and understanding will improve behaviors related to breast cancer and facilitate early presentation and detection and enhance proper management and treatment of breast cancer[14].

A study that examined the delays experienced by patients with breast cancer at two rural Rwandan cancer facilities indicated that patients with breast cancer in Rwanda experience long patient and system delays before diagnosis; these delays increase the likelihood of more advanced-stage presentations[18]. Educating communities and healthcare providers about breast cancer and facilitating expedited referrals could potentially reduce delays and hence mortality from breast cancer in Rwanda and similar settings[18].

Introducing a breast cancer awareness campaign in the Democratic Republic of Congo, based on information by well-educated health care workers, breast self-examination and clinical breast examination, and resulted in an increase of women looking for diagnosis and treatment in the hospital instead of consulting non-medical health care workers like witchdoctors. With an annual or bi-annual information day, knowledge on breast cancer can clearly reach out to more women and with some financial involvement of the government more women can be diagnosed at an earlier stage [19].

Standardization of breast cancer treatment in Uganda:
The Uganda Cancer treatment guidelines:
The Uganda cancer Institute (UCI) has published guidelines for treatment of cancers in Uganda. These guidelines focus on the five most frequently occurring cancers in Uganda, namely Kaposi sarcoma, cancer of cervix, prostate cancer, esophageal cancer and breast cancer which contribute more than 60 percent of all the cancers seen at the Uganda Cancer Institute[8]. After six to twelve months of implementation of these guidelines, the UCI planned to develop another edition encompassing the 10 most frequent cancers in Uganda with the aim of improving cancer care in Uganda and the rest of East Africa[8] .

In regard to breast cancer, the UCI cancer treatment guidelines has recommended surgery, radiotherapy and chemotherapy as the treatment options administered singly or in combination with each other depending on the stage of breast cancer at the time of diagnosis[8].

Surgical options for treatment of Breast cancer in Uganda:
Prophylactic mastectomy, breast conservation and mammographic surveillance are the recommended surgical options offered to women with very high risk of Breast cancer such as those with positive BRCA 1 and BRCA 2 gene mutations[8]. Surgical options have also been provided for lobular carcinoma, ductal carcinoma in situ, breast cancer stages I, II and III, recurrent breast cancer and metastatic breast cancer[8]. Tumour size and accurate pre-surgical assessment of the tumour size itself are independent predictors for the need of a second surgery or even a mastectomy in patients for whom a primary BCS was planned[20].

Ankanbi et al, have argued that of several modalities of treatments available for breast cancers, mastectomy is the most dramatic and traumatic because it involves the removal of an organ of a woman's sexuality and with the attendant risk of marital disharmony. Ina study investigating the perception and the acceptance of mastectomy among male spouses of 108 female patients with breast cancers in Nigeria, less than half (48.1%) of the participants accepted the procedure for their female spouses prior to counseling which rose up to 84.3% after counseling [21]. The higher acceptance rates were determined by Age greater than 65 years (p=0.0274), previous knowledge of mastectomy (p=0.0107) and counseling (p<0.001) while educational status, religion and social class showed no statistical significant difference[21].

Radiotherapy options for treatment of breast cancer in Uganda:
Radiotherapy involves application of radiation to the breast depending on the location and size of the tumor. Different radiotherapy options have been prescribed for different stages of Breast cancer, including breast cancer involving the brain, bone and skin metastases[8]. In March 2016, there was a breakdown of the radiotherapy machine at the Uganda cancer institute and this affected diagnostic and treatment services at the institute affecting treatment of 2000 patients in one week[22], [23]. This led to some patients being referred to Aga Khan International hospital in Kenya, hence the need to strengthen regional capacity in managing cancer cases[24],[25]. A regional cancer registry and treatment protocol for cancer management would be a great step in combating the cancer scourge in the region[8], [25].

Chemotherapeutic treatment options for breast cancer in Uganda:
Approved drugs for treatment of breast cancer in Uganda:
In terms of chemotherapy, a total of 21 standard treatment regimens have been recommended in the Uganda cancer treatment guidelines as the adjuvant hormonal therapy for patients with ER positive breast cancer, regimens for Her2 negative breast cancer, regimens for Her2 positive breast cancer and regimens for recurrent breast cancer in Uganda[8]. The Cancer treatment guidelines recommend 17 drug molecules that should be used alone or in combination with each other for treatments of various types of breast cancer in Uganda[8]. With the exemption of six drugs, the rest are among the 13 drugs approved by the World Health Organization for use in treatment of breast cancer[8],[26],[27],[28]. This is in contrast with 33 drug molecules used in breast cancer treatment approved by the United States Food and Drug Administration[29] [30].

Among the 13 WHO essential drugs approved for use in breast cancer, vinorelbine, carboplatin and Leucoprorelin are not USFDA and only 11 are recommended for breast cancer treatment in Uganda as per established treatment protocols [8][29]. Table 1 shows a comparison of drugs approved for treatment of breast cancer in selected developing and developed countries.

Table 1:- Drugs approved for treatment of breast cancer in the US, Uganda and Kenya in comparison with WHO.

Drug name (Generic)	US-NCI	WHO	UCI Cancer Treatment guidelines	KENYA
Abemaciclib*	Y	X	X	X
Ado-trastuzumab*	Y	X	X	X
Anastrazole*,#	Y	Y	Y	Y
Capecitabine*,#	Y	Y	Y	Y
Carboplatin#	X	Y	Y	Y
Cyclophosphamide*	Y	Y	Y	Y

Docetaxel*#	Y	Y	Y	Y
Doxorubicin(Adriamycin)*,#	Y	Y	Y	Y
Epirubicin*	Y	X	Y	Y
Eribulin mesylate*	Y	X	X	X
Everolimus*	Y	X	Y	X
Exemestane*	Y	X	Y	Y
Fluorouracil*	Y	Y	Y	Y
Fulvestrant*	Y	X	X	
Gemcitabine*	Y	X	Y	Y
Goserelin*	Y	X	Y	X
Ixabepilone*	Y	X	X	Y
Lapatinib*	Y	X	X	Y
Letrozole*	Y	X	Y	Y
Leuprorelin	X	Y	X	X
Megestrol maleate*	Y	X	X	X
Methotrexate*	Y	Y	Y	Y
Neratinib maleate*	Y	Y	X	X
Olaparib*	Y	X	X	X
Paclitaxel*	Y	Y	Y	Y
Paclitaxel Albumin-stabilized nanoparticle formulation*	Y	X	X	Y
Palbociclib*	Y	X	X	X
Pamidronate disodium*	Y	X	X	X
Pertuzumab*	Y	X	X	X
Ribociclib*	Y	X	X	X
Tamoxifen*	Y	Y	Y	Y
Thiopeta*	Y	X	X	X
Toremifene*	Y	X	X	X
Trastuzumab*	Y	Y	Y	Y
Vinblastine*	Y	X	X	X
Vinorelbine	X	X	X	Y

KEY: USNCI = United States of America National cancer Institute, UCI= Uganda Cancer Institute, WHO = World health organization, KNCTG = Kenya National Cancer treatment guidelines, Y = Included among Drugs used for breast cancer; X = Not among the drugs used for breast cancer; * =USFDA approved brand available in the US; # There is a registered brand in Uganda.

Treatment of ER positive breast cancer in Uganda:
Estrogen receptor (ER) expression is the main indicator of potential responses to endocrine therapy (ET), and approximately 70% of human breast cancers (BCs) are hormone-dependent and ER-positive [31]. Eight drug regimens consisting of Tamoxifen, goserelin, anastrazole, letrozole, exemestane, and Everolimus are recommended for treatment of ER positive breast cancer in Uganda[8]. The drugs are used singly or in combination for a period of 5-10 years[8].

Treatment of Her2 negative and Her 2 positive breast cancer in Uganda:
Five combination drug regimens consisting of Adriamycin, Cyclophosphamide, 5-fluorouracil, methotrexate, Epirubicin, cyclophosphamide, Docetaxel and/or paclitaxel are recommended for treatment of Her2 negative breast cancer in Uganda[8]. Whereas the preferred regimen is CAF consisting of Cyclophosphamide, Adriamycin (Doxorubicin) and Flourouracil, other recommended regimens are CMF, FEC, ACT followed by Docetaxel or paclitaxel and TAC[8].

Four drug combinations consisting of Docetaxel, carboplatin, Trastuzumab, doxorubicin, cyclophosphamide and paclitaxel are recommended for treatment of Her2 positive breast cancer in Uganda [8]. The recommended drug regimens are TCH with dose Dense AC followed by paclitaxel and transtuzumab[8].

Four combination regimens and four single agents are recommended for treatment of Her2 positive breast cancer in Uganda. The drugs used are gemcitabine, carboplatin, docetaxel, cyclophosphamide, capecitabine and Paclitaxel[8].

Regulatory approval and availability of antibreast cancer drugs on the Ugandan Market:
Registered brands of antibreast cancer medicines on the Ugandan market:
Regulation of quality, safety and efficacy of drugs in Uganda is by the National drug Authority[32]. Assessment of the drug registration status of the seventeen drug molecules recommended for breast cancer in the Uganda cancer treatment guidelines revealed that there were 39 brands of these drug molecules in Uganda registered by the National drug Authority as of 23rdAugust 2018, accounting for 0.01% of all the registered drugs for human use in Uganda[33].

The registered drugs for breast cancer treatment in Uganda are majorly generics manufactured by 15 pharmaceutical industries based in seven foreign countries with stringent and Non stringent regulatory authorities, namely; United kingdom (8.51%), Germany (10.64%), United states of America (2.13%), India (61.7%), Switzerland (%, n=4), Cyprus/Europe (4.25%) and Italy (2.13%) implying that most of the anti-breast cancer medicines registered and used in Uganda originate in India[33]. These countries also serve as source of 66.6% of other registered drugs for human use in different disease conditions in Uganda[33].

Three out of the 17 drug molecules namely Exemestane, cyclophosphamide and 5-Fluorouracil that are recommended for breast cancer treatment in Uganda did not appear on the Uganda national drug register as of 23rd August 2018[33]. This implies that patients prescribed these drugs for breast cancer treatment had to use un registered brands whose cost and availability on the Ugandan market. This also increases the likelihood of patients being supplied counterfeit drugs as NDA's capacity to detect counterfeits is in question by a some health professionals and pharmaceutical dealers[34].

Counterfeit drugs represent a huge threat to public health because of the high risk of damage they can cause to patients who consume them[35]. It is estimated that over 10% of drugs in circulation in the world are counterfeit, but the rate is much higher in developing countries because of the weakness and lack of drug regulatory systems[35].

Supply system of Antibreast cancer medicines in Uganda:-
Supply system for anticancer drugs in Uganda has been facing challenges with accusations of inflating of prices by the national medical stores and supply of inferior brands and these led to the enactment of the Uganda cancer Institute Act, a law that gives the UCI autonomy in running its functions including planning procurement of drugs.

Importation of antibreast cancer medicines into Uganda can be done by 11 authorized local technical representatives who serve as major distributors of these medicines for 16 license holders[33]. Other local licensed pharmaceutical companies and health facilities can also import these medicines provided the proforma invoice has been endorsed by the authorized local technical representative who registered that particular drug[36],[37]. This has however caused discomfort among retailers of these medicines who feel the process is lengthy and costly. Un registered brands can only be imported when the local technical representative gives a letter of non-availability of the said drug and that there are no registered alternatives on the national drug register at the time of intention to import such a drug.

Budgetary allocation for cancer care in Uganda:
The Government of Uganda allocated UGX 219 billion (UGX=Uganda shillings, 1 GBP = 4826.94 UGX) in 2014/15 towards meeting the annual medicine needs of the country, with 70% of this public expenditure being donor funded and half of this vote allocated to EHMS needs of specialist institutes (cancer, heart and blood transfusion) and other essential medicines other than ARVs/HIV commodities, TB medicines, vaccines, reproductive health commodities and malaria[38].

The Uganda Cancer Institute was been allocated UGX 91.19 billions out of the UGX 2.308 trillions of entire health sector budget for the Fiscal year 2018/2019 implying that the allocation to UCI accounts for 0.36% of the total National budget of 25.1 trillions and with the support of the African development bank, the Uganda cancer institute has been expanded into a centre of excellence with the acquisition of advanced cancer treatment equipment including a linear accelerator (MOFPED, 2018). 70.47% of this budgetary allocation was to be obtained by external funding, expected to cover wages (UGX 4.74 Billions), non-wage recurrent expenditures (UGX10.26 Billions) and domestic development (UGX 11.96 Billions). This resulted into an increase in wages by 30.17%, non-wages by

69.40% and domestic development by 0.25% in comparison to the approved budget for the FY 2017/2018 [39, p. 51].

In terms of developing human resource capacity to manage the challenge of breast cancer and other cancers in the country, the Ugandan Ministry of health has reported that 178 specialists have so far been funded to pursue different courses in cancer related disciplines including 14 specialist oncology fellowships, radio pharmaceutics and doctoral studies[38].

Healthcare providers need training so that they can increase patient education about breast self-examination, conduct clinical breast exams, and sensitively deliver a breast cancer diagnosis. Given the burden of stigma associated with the diagnosis, it is critical to disclose positive test results and subsequent treatment options with care, especially when surgery is indicated. By better understanding the impact such a diagnosis may have on a patient, a trained health professional can communicate a diagnosis and discuss treatment in a manner that is not stigmatizing, but rather inviting of better engagement. Survivor-advocates could potentially assist in the training of health care providers by providing perspectives on what messages from providers will help optimally engage patients in care[16].

Treatment challenges with chemotherapeutic agents for breast cancer:
A successful anticancer drug should kill or incapacitate cancer cells without causing excessive damage to normal cells. This ideal is difficult, or perhaps impossible, to attain and is why cancer patients frequently suffer unpleasant side effects when under-going treatment[39].

Each of the regimens against breast cancer as recommended in the Uganda cancer treatment guidelines is associated with toxicities, and long duration of use affecting adherence to treatment by breast cancer patients and hence the need to effectively counsel patients but also search for alternative treatments against breast cancer[8].

Gakwaya et al have reasoned that adequate counseling, pain and other symptom control should be part and parcel of the entire management strategy; and that good counseling enables the patient and her family to cope with the stress that is part and parcel of cancer as this enables them to adjust their life styles and that counseling should continue during treatment and follow up[40]. This has also been confirmed by Meacham et al who also argue that to engage and stay engaged in care, the importance of effective counseling from a physician, including sensitive disclosure of a positive diagnosis and thorough explanation of the disease, treatment course and prognosis should be emphasized[16].

Ankanbi et al have recommended that health care workers should involve men in breast cancer related education. They observed in a study that spouses of patients with locally advanced diseases accepted mastectomy more readily for their female partners as compared to those with early and metastatic diseases (p<0.001). Furthermore, about 79% of those who accepted the procedure prior to counseling exhibited negative behavior toward their partners[21].

Meacham et al have reported that many breast cancer patients discontinue treatment because of the economic burden[16]. In this study, participants described the difficulty of navigating the health system while trying to afford treatment. There is only one public cancer treatment center in the country, the Uganda Cancer Institute, yet it is not well known. All participants described the challenge of determining where to obtain treatment that would not exhaust their financial reserves. Some shared stories of private doctors exploiting cancer as a "cash cow" and depleting patients' finances while providing inadequate treatment. Difficulty navigating care delays treatment and discourages patients from continuing[16].

Conclusion:-
Breast cancer remains a major disease burden, characterized by delays in diagnosis of breast cancer with majority of patients seeking care at advanced stages and others resorting to the use of herbal medicines. These in addition to the limited availability, inadequate budgetary allocation and patient adherence challenges in regard to the few registered anti-breast cancer medicines recommended as anti-breast cancer regimens account for the reported incidence rates and mortality rates due to breast cancer in Uganda. Staging is based on The American Joint Committee on Cancer TNM system. Surgery, radiotherapy and chemotherapy are the recommended treatment options administered singly or in combination with each other depending on the stage of breast cancer at the time of diagnosis.

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Declaration of conflict interest:

All the authors declare not having any conflict of interest.

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