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RESEARCH ARTICLE

SCREENING POLICIES FOR OVARIAN CANCER IN NIGERIAN HOSPITALS: A REVIEW

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Abstract

Ovarian Cancer is a problem battled worldwide and is typically diagnosed at an advanced stage due to the lack of effective screening strategies. An effective screening method should detect the disease at an earlier stage at diagnosis such that treatment would result in better outcome and not the inevitable mortality. Diagnosis of Ovarian cancer at an early stage (stage 1) could be a benefit of good screening strategies because it is associated with a high 5- year survival rate (95%) as it appears that globally, there is no early detection for this yet. In this article, we review the epidemiology, risk factors as well as the current state of screening tests for ovarian cancer in Nigeria

Introduction:-

In most parts of the world, cancer is the most common cause of death and is currently the worst barrier to achieve the life expectancy goals in most countries. Of the gynecologic cancers that affect women, ovarian cancer is a leading cause of death. In general, it is ranked the fifth most common cause of death among the female gender. After initial treatment of ovarian cancer, there is usually a high rate of recurrence based on the fact that most cases go unnoticed and are only diagnosed at an advanced stage. Often times, most women have no prior knowledge of the possible symptoms, risk factors and the fatal harm that ovarian cancer could cause, hence they suffer mortality from the disease (Arora*et al.*, 2021).

In Nigeria, according to the International Agency for research on cancer, ovarian cancer is the 6th commonest cancer in women and the 2nd commonest genital tract cancer. It accounted for 1723 incident cases in 2012 with estimated age standardized incidence rate of 3.1 per 100,000 women. It is also the 2nd leading cause of female genital cancer related deaths in the country with approximately 1300 deaths in 2012, a crude mortality rate of 3.2% and estimated age standardized mortality rate of 2.5 per 100,000 women (Okunowo&Adaramoye, 2018).

Risk Factors of Ovarian Cancer

Various risk factors are associated with ovarian cancer. It generally affects postmenopausal ladies, where increasing age is related with a higher frequency of occurrence, progressed stage of this disease, and lower survival rates. According to a few case control studies, pregnancy poses a protective role against ovarian cancer, therefore, reducing the risk of developing ovarian cancer of any form.

The presence of ovarian cysts is also a risk factor for ovarian cancer as some benign ovarian cysts can act as a precursor for malignant ovarian tumors.

The greatest risk factor of ovarian cancer is a positive family history of breast or ovarian cancer, where an individual history of breast cancer too elevates the risk (Arora*et al.*, 2021).

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Current State of Screening Tests for Ovarian Cancer in Nigeria

Postmenopausal women and those with a familial history of gynecologic cancers (especially breast and ovarian cancers) are to be subjected to screening at intervals. These are the individuals that are more prone to developing ovarian cancer. However, the lack of proper organization of the health care sector in Nigeria, the ignorance of most women at risk, among other issues usually mean most ovarian cancer cases are diagnosed at an advanced stage, which leads to poor outcomes of this disease(Umar *et al.*, 2016).

In the country presently, screening for ovarian cancer is carried out by conducting transvaginalsonography and CA 125 assay and more often than not, this happens after the symptoms have become very severe (clinical presentations) (Iyoke*et al.*, 2013)

Transvaginal Ultrasound/Sonography (TVS)

Medical ultrasonography has grown to become a basic and necessary part of gynecologic evaluation. The transvaginal route became popular with the introduction of high-frequency probes particularlydesigned for intravaginal use. The higher resolution obtained was found to be more useful in gynecology as the vaginal probe's proximity to the pelvis affords a detailed view. A study by Okeji*et al.*,2017 on the perception and attitude of Nigerian women to transvaginal ultrasound showed that majority of their respondents had a positive attitude to TVS and were also willing to undergo the investigation in future, hence it was acceptable to them. It was however observed that acceptability increased with increasing academic status (Okeji*et al.*,2017). TVS is a very important part of virtually every ovarian cancer screening tests. It is performed with a vaginal probe which generates accurate ovarian images that can be used to detect early changes in physical structure of the ovaries and volume not appreciated on clinical examination.Irregularities in the morphology of the ovary are based on the presence of papillary projections from the cyst wall in a complex cystic ovarian tumor . In premenopausal women, Ovarian volumes >20 cm^3 is defined as abnormal while >10 cm^3 in postmenopausal women is defined as abnormal. TVS is usually conducted in hospitals or diagnostic centers equipped with state of the art ultrasonography machines.

In Nigeria however, TVS for ovarian cancer is only usually done after the symptoms of ovarian cancer is well defined, thus the high mortality rate; due to late detection. Women predisposed to ovarian cancer especially genetically are therefore advised to perform periodic TVS checkups thereby increasing the possibility of arresting the disease at an early stage, increasing the survival probability (95%)(Chesang, 2017).

Cancer Antigen 125 (CA 125) Biomarker

This is a large transmembrane glycoprotein that was first identified in human ovarian cancer cell lines by Bastand colleagues in 1981. CA-125 is currently used in detection as well as monitoring of treatment and follow-up among patients with ovarian cancer. The function of CA-125 is unclear; however, it is thought to promote ovarian cancer tumourigenesis. Unfortunately it lacks sensitivity and specificity. The sensitivity of CA-125 is related to the stage of disease i.e. it is only elevated in 50% of patients with stage I, but 80% – 90% of patients with stages 3 – 4. And it is not specific as is elevated in certain benign conditions such as endometriosis, fibroids, pregnancy, pelvic inflammatory disease, pericarditis, pleurisy, pancreatitis, liver disease, tuberculosis, and peritonitis, and also in malignancies of other sites such as breast and gastrointestinal cancers (Chesang, 2017).

The serum of an individual can be tested for CA-125 at almost any reputable diagnostic center present in Nigeria and the test is most often ordered after symptoms of the disease becomes prominent (in Nigeria).

Clinical Presentations

A study by Okunowo&Adaramoye, 2018 on Women's Knowledge on Ovarian Cancer Symptoms and Risk Factors in Nigeria revealed that knowledge of the symptoms and risk factors of ovarian cancer is very poor among Nigerian women (Okunowo&Adaramoye, 2018). Hence, symptoms of ovarian cancer such as ascites, gastrointestinal dysfunction, abdominal bloating, pelvic pain, shortness of breath, etc., might be initially missed or attributed to other disease processes because they are general and nonspecific. Symptoms become more severe and apparent at the late stages of the disease (Okunowo&Adaramoye, 2018).

A combination of these screening tests usually provide a screening strategy for ovarian cancer patients in Nigeria and they are relatively affordable tests with TVS costing not more than 20,000 Naira and CA-125 blood test costing not more than 15,000 Naira depending on the location.

Ovarian Cancer Screening In Other Parts of The World

It is an established fact that women past the age of menopause are at risk for ovarian cancer. Hence in advanced other parts of the world, post-menopausal women with no familial history of breast or ovarian cancer are usually classified as 'average risk individuals'. They are subjected to screening strategies annually.

Individuals with familial relations to already confirmed breast cancer patients are considered 'high risk patients' based on the fact that mutations of BRCA1 & BRCA2 genes increases the risk of ovarian cancer by 40-50%. This set of individuals undergoes the screening strategies more frequently (every 3-6 months) to monitor the level of indicative factors of ovarian cancer.

Most screening strategies in other parts of the world also utilize TVS and CA-125 serum biomarkers in diagnosing patients with ovarian cancer.

In women with average risk for developing ovarian cancer serum CA-125 levels are checked annually and a baseline for each individual patient is determined. A dramatic increase in CA-125 level above the baseline in subsequent check-ups prompts for the conduction of a TVS screening. If the imaging suggests a possible malignancy, an operation is undertaken. However, if the increase is only moderate, a test is repeated after 3 months. A further elevation triggers TVS screening and possible surgery is the imaging suggests so.

In women that have confirmed the mutations of BRCA1 or BRCA2 genes, TVS and CA-125 tests are usually conducted every six months to monitor the possible occurrence of ovarian cancer.

While the screening tests are generally the same as Nigeria, the measures above are conducted to detect ovarian cancer at a very early stage to increase the survival rate of patients.

In order to increase the specificity and sensitivity of the screening tests, laboratories in the American Association for Cancer Research have been evaluating potential biomarkers such as HE4, CA72.4, CA15-3, CEA, V-CAM1 among others which will be used in combination with CA-125 with the goal of increasing the fraction of early-stage ovarian cancers detected.

The United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOS) provided preclinical serum samples of women destined to develop ovarian cancer from their biobank to a set of investigators in Manchester, UK. They identified 3 panels of biomarkers in combination with CA-125 that detected a fraction of cases missed by CA125 and produced lead time over CA125 of 5–6months to a year or more. The biomarkers are lecithin–cholesterol acyltransferase (LCAT) and insulin-like growth factor-binding protein 2 (IGFBP2)phosphatidylcholine–sterol acyltransferase, vitamin K–dependent protein Z and C-reactive protein ; and HE4, CHI3L1, PEBP4 and/or AGR2 (Robert *et al.*, 2020).

A lot of research and screening trials are ongoing to ensure that a high level of specificity and sensitivity is attained as regards ovarian cancer screening; and also to increase the early detection rates of ovarian cancer, increasing survival rates of ovarian cancer patients all over the world.

Impact of Healthcare In The Management Of Ovarian Cancer In Nigeria

The occurrence of ovarian cancer in women in Nigeria is low when compared to cervical or breast cancer patients. Nigeria launched the National Cancer Control Plan (2018–2022) in 2018 and the goal was to make screening services accessible to all Nigerians by 2022, focusing more on women as they are more predisposed to cancer, and focusing more on breast and cervical cancers, giving little attention to ovarian cancer as a result of its relatively low occurrence rate (Umar *et al.*, 2016). Patients that have developed ovarian cancer in Nigeria have most times being diagnosed at a late stage, this is due to their ignorance to the symptoms/ modes of presentation of ovarian cancer. The study by Okunowo&Adaramoye, 2018 on 'Women's Knowledge on Ovarian Cancer Symptoms and Risk Factors in Nigeria: An Institutional-based Study' showed that knowledge of the symptoms and risk factors of ovarian cancer is still very poor among Nigerian women (Okunowo&Adaramoye, 2018). Most women waste time either by staying at home until symptoms of ovarian cancerbecomeadvanced, severe and very prominent. Time is also usually wasted with the general practitioner treating those nonspecific symptoms which should have been well handled by gynecologic oncologists (Umar *et al.*, 2016).

Political instability, corruption, limited institutional capacity and an unstable economy are major factors responsible for the poor development of the health sector in Nigeria. As a result of this, many patients may have received care and managementthat is below par (Umar *et al.*, 2016).

The number of trained gynecologic oncologists is few in Nigeria and so most often, ovarian cancer patients are usually operated on by general surgeons or gynecologists (Umar *et al.*, 2016). This is a huge burden to the Nigerian healthcare system and it needs to be addressed as soon as possible.

Conclusion:-

Ovarian Cancer is associated with a very high mortality rate in Nigeria as most people are diagnosed at an advanced stage. This is majorly due to failure of affected women to submit themselves for screening at intervals as a result of their negligence and/or ignorance and also the lack of early detection methods for the disease. TVS and CA-125 tests detect the disease with high specificity only in the later stage.

Recommendation:-

More studies should be directed towards developing an adequate early-detection screening algorithm which will help increase the survival rate of women living with ovarian cancer.

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