

# **RESEARCH ARTICLE**

# OVARIAN CANCER: REVIEW OFLITERATURE.

# Isabella Ndege<sup>1</sup>, Xiu-gui Sheng<sup>2</sup>, Anita Kasanga<sup>2</sup> and Davis Nsamba<sup>2</sup>.

- 1. School of Medicine and Life Sciences, Shandong Academy of Medical Sciences, University of Jinan; Shandong Cancer Hospital and Institute, 440 Ji-Yan Road, Jinan 250117, Shandong Province, China.
- 2. Shandong Cancer Hospital and Institute, 440 Ji-Yan Road, Jinan 250117, Shandong Province, China.

# Manuscript InfoAbstractManuscript HistoryThe purpose of this paper is to provide a brief overview of ovarian<br/>cancer. We study several literatureand summarize the prevalence of<br/>ovarian cancer, risk factors, staging, current screening modalities and<br/>advances in therapeutic management to date.

#### Key words:-

epithelial ovarian cancer, screening, treatment, CA125, HE4

Copy Right, IJAR, 2016,. All rights reserved.

#### Introduction:-

Ovarian cancer ranks among the top ten diagnosed cancers and top five deadliest cancers in most countries with the highest mortality (1,2))

.....

Estimated new cases of ovarian cancer in the US in 2014 were 21 980, estimated deaths from ovarian cancer in the US in 2014 were 14 270(3). Two years later, according to research done by the America Cancer society, the number of women estimated to be diagnosed this year has increased to 22 280 and the number of deaths slightly decreased to 14 240. In other words, a woman's risk of getting ovarian cancer during her lifetime is 1/75. Ovarian cancer incidence rates reported from countries with nationwide cancer registration and those from more developed countries are generally similar to each other. In less developed countries and regions, ovarian cancer rates are relatively lower, and this is likely due in part to the lack of quality data from large portions of the population in these countries (4)

Overall, the 5-year survival rate associated with epithelial ovarian cancer, most common histology (90%) of ovarian tumors(6,7), is still less than 30% (5) Ovarian cancer is an international issue. Women from all continents and walks of life are affected. A lot of emphasis used to be put on breast cancer, but medical personnel are now also dividing their attention to what is popularly known as the silent killer.

# **Risk factors for ovarian cancer:-**

#### Factors linked to an increase in ovarian cancer risk include:-

Increasing age -ovarian cancer incidence rates increase with advancing age and range from 0.2 among those aged 0-14 to 29.2 among those aged 75 years and older (1).

Nulliparity-Regarding reproductive factors, studies over several years have consistently associated nulliparity with increased risk of ovarian cancer (8,9)

#### **Corresponding Author:- Xiu-gui Sheng**

Address:- Shandong Cancer Hospital and Institute, 440 Ji-Yan Road, Jinan 250117, Shandong Province, China.

Obesity after menopause: Some studies have suggested a modest increased risk of ovarian cancer in obese women (10), however, others have found no relationship between body mass index and ovarian cancer (11)

#### Early menarche, late menopause:-

Family history of ovarian cancer. At least 10% of all epithelial ovarian cancers are reported to be hereditary, with the majority (about 90%) of these related to mutations in BRCA genes and 10% related to mutations associated with Lynch syndrome (12) Hereditary ovarian cancers have distinct patterns from sporadic ovarian cancers. Many are diagnosed at younger ages and less advanced stages than sporadic ovarian cancers (12)

### Factors linked to a lower risk of ovarian cancer include-:

# Multiparity:-

# Breastfeeding:-

Use of oral contraceptives: Some studies have shown a protective effect of oral contraceptives on ovarian cancer (13,14), but IARC classifies estrogen, combined estrogen-progesterone oral contraceptives, and combined estrogen-progesterone hormone replacement therapy as class one carcinogens (15,16). More studies need to be carried out.

A hysterectomy and tubal ligation: They are associated with decreased risk. Tubal ligation has been estimated to decrease risk substantially (RR= 0.33, 95% CI 0.16 to 0.64), while hysterectomy may have a weaker, but still protective association (RR= 0.67, 95% CI 0.45 to 1.00) (17)

#### Signs and symptoms:-

Ovarian cancer is a killer disease with an insidious onset of symptomswhich by the time they present, the disease is at advanced stage, thus increased mortality and morbidity. The symptoms are because of either increase in size of the tumor thus applying pressure to other organs or metastasis to other body parts. Some of the common symptoms include abnormal vaginal bleeding, pain in the pelvic or abdominal area, back pain, bloating, while eating, changes in appetite, often a loss of appetite , feelings of pressure in the pelvis or lower back increased urinary frequency, changes in bowel movements .

#### Screening:-

Their is lack of adequate screening tests for early stage ovarian cancer. Medical professionals rely on clinical symptoms, imaging studies and measurement of serum CA125 levels to diagnose possible ovarian cancer and because of the silent nature of the disease, most patients present with advanced disease.

CA125 is a glycoprotein antigen whose elevation often precedes clinical evidence of relapse by imaging or physical examination in roughly 80% of patients with ovarian cancer. It has low specificity, particularly in premenopausal women, and could also be elevated above normal in a number of benign gynecological conditions and in other malignancies (18-21) and as such human epididymis protein 4 (HE4), a new biomarker found in the serum of patients with EOC, and mainly expressed in serous and endometrioid cancers EOCs(26,27,28) is now gaining ground in clinical practice, especially in differential diagnostics (22,23). In combination with CA125, it has shown promising results in the differential diagnosis of benignand malignant pelvic masses(22,24,25)

#### Staging:-

According to the International Federation of Obstetrics and Gynecology (FIGO)(45); stage I, growth is limited to the ovaries while in stage II, it involves one or both ovaries, with pelvic extension and/or primary peritoneal cancer. Advanced disease refers to stage III and IV. In stage III,tumor involves one or both ovaries, with histologically confirmed spread to the peritoneum outside the pelvis, and/or metastasis to the retroperitoneal lymph nodes while in stage IV itinvolves distant metastasis, excluding peritoneal metastasis.

#### **Treatment:-**

Surgery is able to treat early stage disease. The five-year survival rate for early-stage (stage I or II) ovarian cancer is around 90% [29]. Adjuvant chemotherapy for early stage ovarian cancer is still controversial but some studies have shown its benefit under confined conditions(30).

The standard treatment for patients with advanced ovarian cancer is maximal surgical cytoreduction (total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy and omentectomy) followed by systemic platinum-based chemotherapy and, actually, is reasonable to expect a 5-year

survival for 10-30% of women diagnosed with ovarian cancer at stage III or IV (31). The concept of primary debulking surgery is to diminish the residual tumor burden to a point at which adjuvant therapy will be optimally effective. The percentage of patients with advanced ovarian cancer who can optimally undergo cytoreductive surgery seems to range from 17%-87% (32). When deciding debulking surgery, we should assess predictive factors with respect to residual macroscopic disease after debulkingsurgerywhich is the strongest independent variable in predicting survival (33). As such, the choice of a surgeon is of utmost importance(34,35). Ovarian cancer patients should be referred to gynecology oncologists.

# **Conclusion:-**

Ovarian cancer is indeed a big concern in the medical field. Research centers for ovarian cancer should be enabled and encouraged as they continue their search for ways of managing this deadly disease. Medical personnel should always be alert when patients present with gynecological problems and above all, should maintain a positive attitude.

# **References:-**

- Ferlay J.; Shin H.R.; Bray F.; Forman, D., Mathers, C. &Parkin, D.M. (2008) GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010.
- 2. Bertone-Johnson ER. Epidemiology of ovarian cancer: a status report. Lancet. 2005; 365: 101-102(PubMed)
- 3. Cancer statistics, 2014 Rebecca Siegel MPH, Jiemin Ma PhD, ZhaohuiZou MS and AhmedinJemal DVM, PhD.
- 4. Sherri L. Stewart Ovarian Cancer Incidence: Current and Comprehensive Statistics
- 5. Andersen MR, Goff BA, Lowe KA, et al (2008). Combining a symptoms index with CA125 to improve detection of ovarian cancer. *Cancer*, **113**, 484-9.
- 6. Chen, V.W.; Ruiz, B.; Killeen, J.L.; Cote, T.R.; Wu, X.C. & Correa, C.N.(2003) Pathology and classification of ovarian tumors. *Cancer*, Vol 97, No. 10 Suppl., (May 2003), pp. (2631-2642)
- 7. Goodman, M. T. & Howe, H. L. (2003). Descriptive epidemiology of ovarian cancer in the United States, 1992-1997. *Cancer*, Vol 97, No. 10 Suppl., (May 2003), pp( 2615-2630).
- 8. Modan B, Hartge P, Hirsh-Yechezkel G, et al. Parity, oral contraceptives, and the risk of ovarian cancer among carriers and noncarriers of a BRCA1 or BRCA2 mutation. N Engl J Med 2001;345:235-240
- 9. Risch HA, Jain M, Marrett LD, Howe GR (1994) Dietary fat intake and risk of epithelial ovarian cancer. JNCI86: 1409–1415
- 10. Leitzmann, M. F.; Koebnick, C.; Danforth, K.N.; Brinton, L.A.; Moore, S.C.; Hollenbeck, A.R.; Schatzkin, A. & Lacey, J. V. (2009), Body mass index and risk of ovarian cancer. Cancer, Vol.115, pp (812–822).
- 11. Fairfield, K.M.; Willett, W.C.; Rosner, B.A.; Manson, J.E.; Speizer, F.E.; & Hankinson, S.E. (2002). Obesity, Weight Gain, and Ovarian Cancer. *Obstetrics & Gynecology* Vol 100, No. 2, (pp. 288–296)
- 12. Prat, J.; Ribé, A. &Gallardo A. (2005). Hereditary ovarian cancer. *Hum Pathol.*, Vol. 36, No. 8, (August 2005), pp. (861-70).
- 13. Beral, V.; Doll, R.; Hermon, C.; Peto, R. & Reeves, G. (2008). Ovarian cancer and oral contraceptives: collaborative: reanalysis of data from 45 epidemiological studies including 23, 257 women with ovarian cancer and 87, 303 controls.Lancet, Vol. 371, No. 9609, (2008), pp. (303-14)
- 14. Narod SA, Risch H, Moslehi R, et al. Oral contraceptives and the risk of hereditary ovarian cancer. N Engl J Med 1998;339:424-428
- IARC (2007). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Combined Estrogen-Progestogen Contraceptives and Combined Estrogen- Progestogen Menopausal Therapy. Vol 91. ISBN 9789283212911
- 16. Modan B, Hartge P, Hirsh-Yechezkel G, et al. Parity, oral contraceptives, and the risk of ovarian cancer among carriers and noncarriers of a BRCA1 or BRCA2 mutation. N Engl J Med 2001;345:235-240
- 17. Hankinson, S.E.; Hunter, D.J.; Colditz, G.A.; Willett, W.C.; Stampfer, M.J.; Rosner, B.; Hennekens, C.H. &Speizer, F.E. (2003) Tubal ligation, hysterectomy, and risk of ovarian cancer. A prospective study. *JAMA*, Vol. 270, No. 23, (December 2003), pp.(2813-2818).
- Park Y, Lee JH, Hong DJ, Lee EY, KimHS. Diagnostic performances of HE4 and CA125 for the detection of ovarian cancer from patients with various gynecologic and non-gynecologic diseases. ClinBiochem. 2011;44(10–11):884–8.

- Hellstrom I, Hellstrom KE: SMRP and HE4 as biomarkers for ovarian carcinoma when used alone and in combination with CA125 and/or each other. AdvExp Med Biol 2008, 622: 15–21. 10.1007/978-0-387-68969-2\_2
- 20. Rosen et al., 2012; Maggino et al., 2013) Rosen DG, Wang L, Atkinson JN, et al (2005). Potential markers that complement expression of CA125 in epithelial ovarian cancer. *GynecolOncol*, **99**, 267-77.
- 21. Miralles C, Orea M, Espana P, et al (2003). Cancer antigen 125 associated with multiple benign and malignant pathologies. Ann SurgOncol, **10**, 150-4 )
- 22. Moore RG, Brown AK, Miller MC, et al. The use of multiple novel tumor biomarkers for the detection of ovaria carcinoma in patients with a pelvic mass. GynecolOncol. 2008;108:402-408.
- 23. Moore RG, McMeekin DS, Brown AK, et al. A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a
- 24. pelvic mass. GynecolOncol. 2009;112:40-46
- 25. Huhtinen K, Suvitie P, Hiissa J, Junnila J, Huvila J, KujariH, et al. Serum HE4 concentration differentiates malignant ovarian tumours from ovarian endometriotic cysts. Br J Cancer. 2009;100(8):1315–9.
- 26. Park Y, Lee JH, Hong DJ, Lee EY, KimHS. Diagnostic performances of HE4 and CA125 for the detection of ovarian cancer from patients with various gynecologic and non-gynecologic diseases. ClinBiochem. 2011;44(10–11):884–8.
- 27. Bouchard D, Morisset D, Bourbonnais Y, et al (2006). Proteins with whey-acidic- protein motifs and cancer. *Lancet Oncol*, **7**, 167-74.
- 28. Devan SM, Pailoor J, Sthaneshwar P, et al (2013). Pattern of tissue expression of CA-125 and HE4 in primary epithelial ovarian tumours and correlation with serum CA-125 Levels. *Asian Pac J Cancer Prev*, **14**, 4545-8.
- 29. Drapkin R, Henning von Horsten H, Lin Y, et al (2005). Human epididymis protein 4 (HE4) is a secreted glycoprotein that is overexpressed by serous and endometrioid ovarian carcinomas. *Cancer Res*, **65**, 2162-9
- 30. Hennessy BT, Coleman RL, Markman M: Ovarian cancer. Lancet. 2009, 374: 1371-82. 10.1016/S0140-6736(09)61338-6.
- 31. Trimbos JB, Parmar M, Vergote I, et al: International Collaborative Ovarian Neoplasm trial and Adjuvant ChemoTherapy In Ovarian Neoplasm trial: two parallel randomized phase III trials of adjuvant chemotherapy in patients with early-stage ovarian carcinoma. J Natl Cancer Inst. 2003, 95: 105-112.
- 32. Hennessy BT, Coleman RL, Markman M: Ovarian cancer. Lancet. 2009, 374: 1371-82. 10.1016/S0140-6736(09)61338-6.
- Ramirez I, Chon HS, Apte SM: The Role of Surgery in the Management of Epithelial Ovarian Cancer: Role of Surgery. http://www.medscape.com/viewarticle/738258\_3
- 34. Vergote I, Trope CG, Amant F, et al: Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med. 2010, 363: 943-953. 10.1056/NEJMoa0908806.
- 35. Giede KC, Kieser K, Dodge J, Rosen B. Who should operate on patients with ovarian cancer? An evidencebased review. GynecolOncol. 2005; 99:447-461.