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The Silent Killer - Ovarian Cancer

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ABSTRACT:

The seventh most typical cancer in women worldwide and the tenth most typical in China is ovarian cancer (OC). With five primary histotypes that differ in origin, aetiology, genetic changes, risk factors, and prognosis, epithelial OC is the most common pathologic subtype. Rare, high- to moderate-penetrance hereditary mutations are the main cause of genetic vulnerability.

Additionally, 29 common susceptibility alleles for OC, including 14 subtype-specific alleles, have been found through genome-wide association analyses. Parity, oral contraceptive use, and breastfeeding are a few reproductive and hormonal factors that may reduce risk, while hormone replacement treatment and later age at menopause raise risk. These connections vary by histotype, particularly for mucinous OC, and are probably due to different etiologies. Similar and distinctive patterns of associations between increased risks for endometriosis-positive women and decreased risks for tubal ligation are shared by endometrioid and clear cell OC. Less is known about the OC risks connected to other gynaecological conditions and procedures like polycystic ovarian syndrome, pelvic inflammatory disease, and hysterectomy. Environmental and lifestyle factors, such as exposure to asbestos and talc powder, are additional potential risk factors.

Keywords : ovarian cancer, symptoms, risk factors, diagnosis, treatment.

Introduction:

Ovarian cancer , "**the Silent Killer"** , which begins in the female that produce ovaries. It often goes undetected until it has spread within pelvis and stomach.At this stage , ovarian cancer is more difficult to treat and can be fatal. It often has no symptoms in early stages,but later this stages are associated with symptoms that can be non specific. It is one of the most common causes of cancer related deaths in women of developed nation. Ovarian cancer leads to death in the women who are diagnosed with gynaecological cancers. Among various causes in women ovarian cancer is fifth most frequent cause which even leads to death. Near about 239,00 new cases of ovarian cancer and 152000, are estimated per year in the world wide.In Eastern and central Europe near about 11.4 per 100,000 and 6.0 per 100,000 cases are seen which is highest rate.whereas China has relatively low rate of incidence that is (4.1 per 100,000).In USA 21,290 cases and 14,180 related deaths are estimated.The risk of developing ovarian cancer in women is 1 in 75 whereas,her chance of dying is 1 in 100.This cancer is extremely hard to diagnose in the early stages and mostly gets detected in advanced stages.At present the screening tests used are not efficiently useful in the ovarian cancer detection.There are some keys for the detection of this cancer which are vaginal ultrasound,biomarker CA-125 which too have failed to prevent the highest rates of death's which are caused by this cancer.Mostly preferred treatment used is chemotherapy in which cisplatin is a choice of drug.Drugs which has been bit successful in curing this cancer at present is antiangiogenic bevacizumab along with poly ADP ribose polymerase inhibitors.Effective prevention,diagnostic techniques is required for the prevention of ovarian cancer.

Etiology:

There are several factors which are associated with the ovarian cancer.post menopause gets mostly affected in women with increasing qge associated with increased incidence also lowers the survival rate.ovarian cancer has the strongest risk factor that is positive family history.various studies has also detected risk of smoking which leads to risk of epithelial tumours.There are specific symptoms related to ovarian cancer which is localized which results into advancement at the time of diagnosis.Lifetime risk of ovarian cancer is 1/7 (1.4%)of the genetic causes are (BRCA1 and 2) and HNPCC (hereditary non polyposis colorectal cancer).Hormonal effects pregnancy,breast feeding,are protective against ovarian cancer.The risk factors for ovarian cancer are late menopause,early Menarche,drugs fir ovulation induction,etc.Endometrosis is also one of the increased risk factor

Epidemiology :

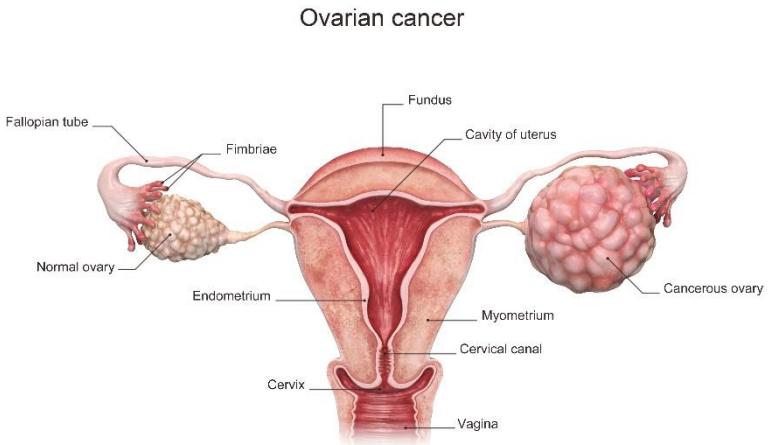
Ovarian cancer ranks 5th in cancer which causes death in women.Risk of women getting ovarian cancer is about 1 in 78 and her chance of dying in her lifetime from ovarian cancer is about 1 in 108.In the year 2020 ,21750 new ovarian cases are been found in which 1.2% are of all cancer cases.The

no. of death's which are estimated were 13,940.The relative survival rate in the 5yr is expected 48.6% among 15.7% of the ovarian cancer cases are diagnosed at very local stage and 58% at metalized stage.According to the US standard population that is 11.1 in 2012 and 2016.There is highest rate of incidence in the Hispanic whites (11.6 per 100,000) subsequently Amaska natives and American Indian (10.3 per 100,000) Asian and Pacific Islanders and Hispanic blacks.Majority 90% of ovarian cancers are found to be epithelial ovarian cancers.based upon the statically models of analysis adjust rate of ovarian cancer are on reducing rate.The developed parts like North America,Central and Eastern Europe has highest age adjusted incidence rates generally 8 per 100,000 followed by South America (5.8 per 100,000) and Asia and Africa lowest (<3per 100,000).The countries which are migrated with low rates to those of highest rates leads to greater risk-Based on the incidence and mortality mimic it is observed that the rate are highest among intermediate for Hispanic

It is lowest among Asians and blacks.Whereas,larger countries such as China impersonates variation with mortality and variation is greater in developed urban regions and less developed rural regions.The developed countries like North America and Europe the mortality and incidence of ovarian cancer is gradually decreased since 1990's.Similarly,the countries which are less developed with recent economic growth and Changes in their lifestyle noticed incuased in mortality rates.

Pathophysiology:

When mistakes in ovarian cell development occur, ovarian cancer develops. Cells often die as they are old or injured, and new cells replace them. When damaged or ageing cells do not degrade as they should, cancer begins to grow. An ovarian tumour or growth is a lump of tissue that develops when there is an accumulation of excess cells. These cancer cells are genetically aberrant and develop uncontrollably as a result. The egg follicle ruptures and transforms into the corpus luteum when an ovary releases an egg. Cell division in the ovary is required to restore this structure. Long-term continuous ovulation necessitates more ovarian repair by dividing cells, which might result in mutations in individual cells.Overall, NF1, BRCA1, BRCA2, and CDK12 gene alterations are most frequently seen in ovarian cancer patients. Microsatellite instability is common in a number of genes, including both oncogenes (most prominently BRAF and KRAS) and tumour suppressors (most prominently PTEN), in Type I ovarian tumours, which are frequently less aggressive. KRAS, BRAF, ERBB2, PTEN, PIK3CA, and ARID1A mutations are the most prevalent ones in Type I tumours. The most dangerous type of cancer, type II, is characterised by the mutation of several genes, including p53, BRCA1, and BRCA2. KRAS mutations are more common in low-grade malignancies than p53 mutations are in cancers of any grade that arise from tumours with limited malignant potential. While Type II cancers can arise from a serous tubal lesion, Type I cancers typically grow from precursor lesions.Serous carcinomas which have BRCA polymorphisms this not only inherently have p53 genetic alterations, specifying that the disposal of both useable genetic makeup is significant for illness to growth.In 50% of high-grade serous tumors, mismatch repair DNA rebuild is corrupt and inefficient, as are slot and FOXM1 pathways. They also often have p53 polymorphisms. Side than in this, point mutation in high-grade serous adenomas are incredibly difficult to describe beyond their high level of gene mutations. BRCA1 and BRCA2 are extremely important for pcr amplification DNA , genetic changes within those genetic material are found in about 15% of ladies with bowel cancer. The most typical polymorphisms in BRCA1 and BRCA2 are the warpdrive genetic alterations that started in a slight pioneering inhabitants of Ashkenazi Jews.Almost 100% of relatively uncommon mucinous colon cancer have genetic changes in KRAS and secondary effects of ERBB2 (often known as Her2 neu). Overall, 20% of polycystic ovary carcinomas have polymorphisms in Her2 / neu.Serous squamous cell carcinoma may grow from serous fallopian tube endometrial malignant tumors, then instead of emerging randomly from gynecologic. Side colon cancer grow from midbrain participation conidia, and that are communities of endometrial hormonal microglia inside the extracellular matrix.



Signs and Symptoms:

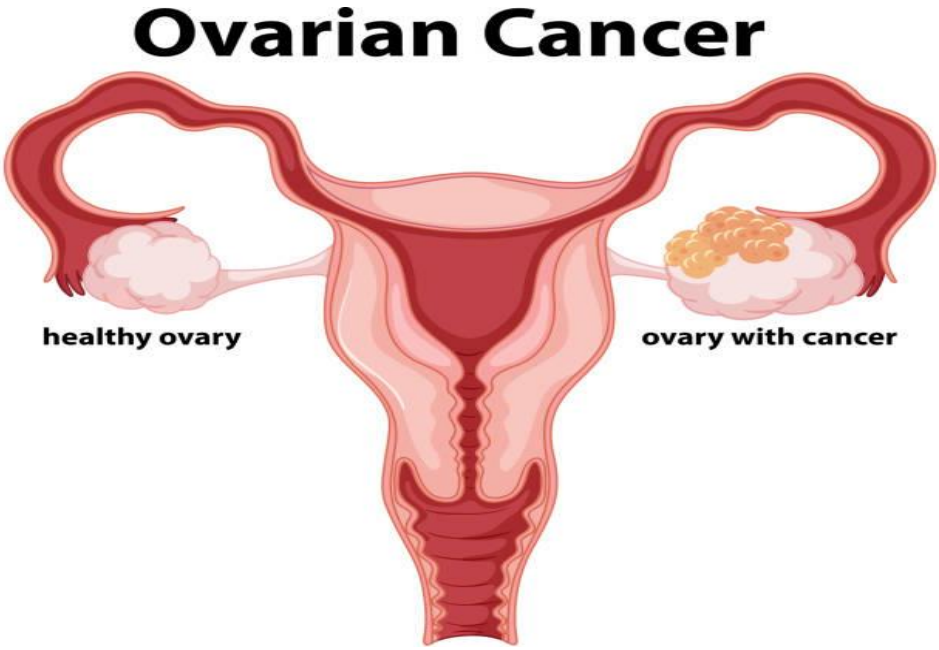
The ovarian cancer when develops it may not cause any noticeable symptoms.the symptoms when happen attributed to some other common conditions such as,Early anxiety,Fatigue,Back pain,Loss of apetite,Nausea,change in bowel movement,abdominal fullness,loss of weight,urinary symptoms,dyspareunia,bloating,ataxia,dysarthia,nystagmus vertigo,diplopia,etc. These symptoms are not clearly understandable before the diagnosis of ovarian cancer.it also includes, increase in level of parathyroid hormone releasing protein which can results into hypercalcemia,this can manifest the mental status,abdominal pain also increases frequency in thirst and urine.

Risk factors:

There are several risk factors which may be the risk of women developing ovarian cancer.Developing an ovarian cancer is also related to amount of time a women spends ovulating.The increased no. of ovulatory cycles results into developing ovarian cancer.During ovulation cells divides by stimulating.If the division of cells are abnormally regulated the tumour may be from which can also be malignant.one of the risk factor for developing ovarian cancer is early menarche(<12yrs)and late menopause (>50 yrs)which increases the no. of ovulatory cycles.Whereas,during suppressed pregnancy or not having children can also results into ovarian cancer.therefore,the women who have not borne children has more risk of ovarian cancer than that of women who have.Hormone replacement therapy or obesity can also raise the risk of ovarian cancer.There is less risk of ovarian cancer in the women who have no or fewer menstrual cycles or the women who have taken oral contraceptives which have pregnancy at an early age or have multiple pregnancies.The women who have/had tubal ligation (surgical procedure for female sterilization by severity of tying fallopian tubes),or by removing the uterus ,ovaries (hysterectomy).Age can also be one of the risk factor for ovarian cancer.The non-genetic factors like high body mass,DM index,alcohol consumption,can also cause ovarian cancer.BRCA1 and BRCA2 are the mutations in gene which are associated with ovarian cancer.They were first discovered in 1994,1995 which mostly influenced ovarian cancer in women.the insertion of the genes can results into inhibition of codon prematuring and the production of proteins becomes shorter.Therefore,the mutations BRCA1 and BRCA2 can results into 50 percent and 20 percent ovarian cancers respectively.

Diagnosis:

Diagnosis of bowel cancer usually begins with a medical examination (including a perineum analysis), a routine blood (for CA-125 and then sometimes side reference points), and ultra sound. Sometimes a villous evaluation is also used to help organize a multiple surgeries.The diagnosis should be acknowledged with operation to inspect the large intestine, take blood tests (samples for light microscope interpretation), and seek tumor cell in the mediastinal fluid. This determines if an carcinoma wide spread is adenoma or virulent. Ovarian cancer's initial stages (I / II) are tricky to assess although most illnesses are qualities and attributes as it is of limited value in identification; consequently, it is infrequently successfully treated until it grows and develops to final phases (III / IV). Additionally, side affects of bowel cancer may correct shape to ulcerative colitis. In girls upon whom prenatal is probability, BHCG echelon can really be tested during the treatment task. Plasma levels alpha-fetoprotein,neuron-specific glycolysis can really be reasoned in girls and women and children and teenagers with assumed benign cysts as younger females with prostate cancer are more likely to have malicious gliomas. The diagnosis of this condition requires both a physical examination, which includes a pelvic examination, and a pelvic ultrasound (either transvaginal or otherwise). A physical examination may reveal increased abdominal girth and/or ascites (fluid within the abdominal cavity), whereas a pelvic examination may reveal an ovarian or abdominal mass.A major finding that frequently suggests ovarian cancer is an adnexal mass, particularly if it is fixed, nodular, irregular, solid, and/or bilateral. However, there are other benign causes of adnexal masses, such as ovarian follicular cyst, leiomyoma, endometriosis, ectopic pregnancy, hydrosalpinx, tuboovarian abscess, ovarian torsion, dermoid cyst, cystadenoma (serous or mucinous), diverticular or appendiceal abscess, nerve sheath tumour, pelvic kidney. In postmenopausal women, the presence of palpable ovaries is another indicator of ovarian cancer. A digital rectal exam and a breast exam may also be included in a physical examination for ovarian cancer suspicion. Lymphadenopathy, a sign of metastasis, may be felt when the supraclavicular, axillary, and inguinal lymph nodes are palpated. A pleural effusion, which can be heard on auscultation, may also be another sign. A small number of laboratory tests are recommended when an ovarian cancer is one of the possible diagnoses. It is customary to get a full blood count and serum electrolyte test;when an ovarian cancer is present, these tests frequently reveal a high number of platelets (20–25% of patients) and low blood sodium levels as a result of chemical signals generated by the tumour. A granulosa cell tumour may be detected by an inhibin A and inhibin B test that is positive. Due to its very poor sensitivity and specificity, a blood test for the marker molecule CA-125 is useful for differential diagnosis and disease follow-up, but it has not been demonstrated to be a viable tool to screen for early-stage ovarian cancer. Premenopausal women with CA-125 levels over 200 U/mL and postmenopausal women with any rise of CA-125 above 35 U/mL may both have ovarian cancer. Given that half of patients with stage I ovarian cancer have a normal CA-125 level, CA-125 values are not reliable indicators of early-stage ovarian cancer.Additionally, benign (non-cancerous) conditions like endometriosis, pregnancy, uterine fibroids, menstruation, ovarian cysts, systemic lupus erythematosus, liver disease, inflammatory bowel disease, pelvic inflammatory disease, and leiomyoma can cause an increase in CA-125 levels. HE4 despite not having undergone rigorous testing, is another potential for ovarian cancer testing. CA19-9, CA72-4, CA15-3, immunosuppressive acidic protein, haptoglobin-alpha, OVX1, mesothelin, lysophosphatidic acid, osteopontin, and fibroblast growth factor 23 are additional tumour markers for ovarian cancer. In order to increase diagnostic accuracy, current research is examining how to take tumour marker proteomics into account in conjunction with other disease indications (such as radiography and/or symptoms). The problem with this strategy is that ovarian cancer has a disparate prevalence, making it likely that tests with extremely high sensitivity and specificity will still produce a significant number of false positive results. This could result in problems like performing operations where cancer is not discovered intraoperatively. Ovarian cancer has not yet been studied using genomics.



Prevention:

In order to prevent ovarian cancer, women with a high genetic risk may want to have their ovaries surgically removed. This is frequently done once a woman has finished having children. This lowers the likelihood that high-risk women will develop ovarian cancer (by about 96%) and breast cancer (by about 50%). Since they also have a higher risk of developing Fallopian tube cancer, women with BRCA gene mutations typically also have their Fallopian tubes removed at the same time (salpingo-oophorectomy). However, due to the method of study, these statistics might exaggerate the risk reduction. A genetic counsellor is frequently recommended to women with a strong family history of ovarian cancer to determine whether it would be advantageous to test for BRCA mutations. Oral contraceptive usage, the absence of menstrual "periods," and tubal ligation all lower the risk.Ovarian stimulation during infertility therapies and the potential development of ovarian cancer may be related Ovarian malignancies have been associated with endometriosis.There no evidence that using talc,smoking,or human papillomavirus infection raises thr risk of developing ovarian cancer. control of weight. Discuss weight management strategies with your doctor if you are overweight or obese taking contraceptive tablets. According to estimates, women who have used birth control tablets for at least five years had a 50% decreased risk of developing ovarian cancer. Years after you stop taking combination birth control tablets, risk is lowered.Alternatives to hormone replacement treatment must be found (HRT). After menopause, you might want to discuss alternatives to HRT with your doctor.conceiving a child and nursing. With each birth, the chance of ovarian cancer reduces. Furthermore, the incidence of ovarian cancer is believed to be reduced by 2% per month of nursing.Undergoing preventative surgery,Some gynaecological procedures, such as tubal ligation, removal of the uterus (hysterectomy), removal of the ovaries, fallopian tubes, or both (salpingo-oophorectomy), which can also occur during a hysterectomy, can reduce the risk of ovarian cancer. These items each have various advantages and dangers. Additionally, while some require surgery, others are rather simple to follow. As a result, some preventive measures might not be suggested.

Treatment:

1.Treatment-Surgery and chemotherapy are frequently used in the treatment of ovarian cancer. In some circumstances, different treatments might be applied.

2. Surgical procedures for ovarian cancer removal include-surgical removal of one ovary. Surgery may entail removing the affected ovary and its fallopian tube in cases of early-stage cancer that hasn't spread past one ovary. Your ability to become a parent may be preserved by this procedure. ovaries are removed via surgery. Your surgeon may remove both of your ovaries and both of your fallopian tubes if you have cancer in both of your ovaries but there are no other visible signs of the disease. Your uterus is left intact after this procedure, so you might still be able to conceive using your own frozen embryos or eggs or eggs from a donor. ovaries and uterus are both removed during surgery. The ovaries, fallopian tubes, uterus, nearby lymph nodes, and a fold of fatty abdominal tissue will be removed by your surgeon if your cancer is more advanced or if you don't want to preserve your ability to have children, advanced cancer surgery. Your consultant doctor might advised surgery to remove as much of the cancer as possible if it has increased. In this case, chemotherapy may sometimes be administered either before or after surgery.

3. Chemotherapy-

Chemotherapy is a medication therapy that employs chemicals to destroy the body's rapidly proliferating cells, especially cancer cells. Chemotherapy medications can be ingested or injected into a vein.After surgery, chemotherapy is frequently administered to eradicate any cancer cells that could have

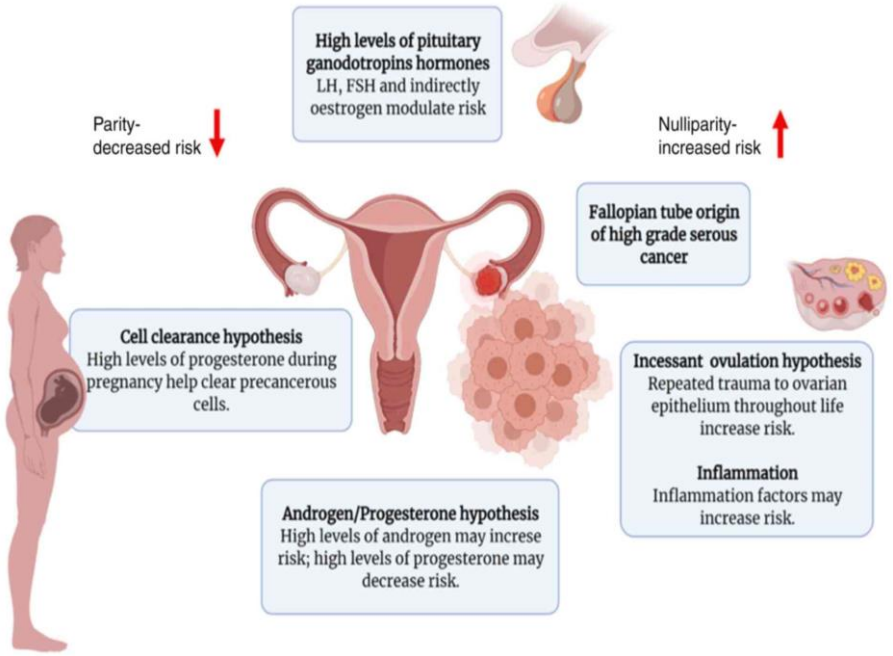
persisted. Additionally, it can be applied before surgery Occasionally, during surgery, chemotherapy drugs may be heated and infused into the abdomen. Before being drained, the drugs are left in place for a specific period of time. The procedure is then over.

4. Targeted treatment-

Targeted medication therapies concentrate on particular flaws in cancer cells. Targeted drug therapies can kill cancer cells by targeting these vulnerabilities.Your doctor may perform a cancer cell test if you're thinking about receiving targeted therapy for ovarian cancer to identify the targeted therapy that has the best chance of working.

5.Hormone Treatment-

Drugs are used in hormone therapy to stop the impact of the hormone oestrogen on ovarian cancer cells. Since some ovarian cancer cells rely on oestrogen to help them grow, inhibiting oestrogen may aid in the management of the disease.Some types of slow-growing ovarian cancers may be treated with hormone therapy. If the cancer returns following initial treatments, it might also be an option.



6.Palliative (supportive) care-

Palliative care is a type of specialist medical treatment that concentrates on relieving pain and other severe sickness symptoms.Experts in palliative care cooperate with you, your beloved ones, and your other medical professionals to add an extra layer of offering to your occuring treatment. While receiving more invasive therapies like surgery and chemotherapy, palliative care can be used.People with cancer may feel better and live longer when palliative care is utilised in addition to all other necessary therapies.A group of doctors, nurses, and other specially qualified professionals offer palliative care. Teams providing palliative care work to enhance the quality of life for cancer patients and their families. This type of treatment coexists with curative

Research:

1.Screening-Hysteroscopy screening is being developed to gather cell samples for histological analysis. This is comparable to the pap test now used to find cervical cancer.The UK Collaborative Trial of Ovarian Cancer Screening is evaluating a screening method that combines transvaginal ultrasonography with CA-125 blood tests.Other research imply that this screening method might be successful.There was some evidence that screening may ultimately save lives, even though the 2015 results were not definitive.The experiment has therefore been prolonged, and its conclusive findings will be released at the end of 2019.One significant issue with screening is that it may not always be possible to discern a clear development of the disease from stage I (noninvasive) to stage III (invasive).

2.Analysis of prognosis-Additionally, there is ongoing research into a number of ovarian cancer prognostic factors. According to recent studies, thrombocytosis indicates cancer with a lower chance of survival and a later stage.Additionally, current studies are examining the advantages of surgery for recurrent ovarian cancer.

3.Immunotherapy-Despite being a topic of active research, there is currently insufficient solid proof that immunotherapy is useful in treating ovarian cancer.However, studies of the VEGF inhibitor and antibody bevacizumab, which can reduce the formation of new blood vessels in cancer, have yielded encouraging results, particularly when combined with the blood vessel-slowing drug pazopanib. Bevacizumab has shown promising results in

early studies on cancer patients with stages III and IV and has been reported to have at least a 15% response rate.Investigations are focused on mucinous ovarian tumours in particular.

4.**Pharmacology**-In the 2000s and 2010, mTOR inhibitors were a heavily researched prospective treatment, however the side effects of these medications (especially hyperglycemia and hyperlipidemia) were poorly tolerated, and the survival benefit was not established. Although PI3 kinase inhibitors have generated interest, they can have serious side effects, including diarrhoea. Selumetinib, a MAPK inhibitor, is another medication under investigation. It increased survival, although there was no connection to any tumour alterations. Bevacizumab can also be used in combination with platinum treatment, which has shown promising early results in PFS but conflicting outcomes in overall survival. The side effect profile of these medications, which includes proteinuria and elevated blood pressure, is one drawback. The medication may potentially aggravate bowel conditions, causing fistulae or intestine perforations. Clinical trials are also being conducted on vintafolide, an antifolate conjugated with vinblastine that may be helpful given that many ovarian tumours have overexpressed folate receptors. Trastuzumab is a potential immunotherapy that is effective against tumours with Her2/neu mutations. Additionally being researched as potential ovarian cancer treatments are other angiogenesis inhibitors. Combining pazopanib and combretastatin is being studied as a treatment for recurrent ovarian cancer. Other angiogenesis drugs include trebananib and tasquinimod. Research is currently being done on a regimen of 3 cycles of carboplatin and etoposide as an alternative to BEP treatment for germ cell cancers.In the 2000s and 2010s, intraperitoneal chemotherapy was being researched for its potential to give tumours larger doses of cytotoxic agents. Although it does improve survival, preliminary trials with cisplatin and paclitaxel have revealed it is not well tolerated, and more acceptable regimens are being developed.Both paclitaxel and cisplatin are being studied as intraperitoneal chemotherapy drugs. Irinotecan in combination with cisplatin is a specialised chemotherapy treatment that is being researched for uncommon clear-cell malignancies.Early trials of PARP inhibitors have also been encouraging, especially in patients with BRCA gene mutations because the BRCA protein interacts with the PARP pathway.

5. **Radiations and hormones**-Current studies on ovarian cancer focus on hormone therapy, specifically the benefits of several drugs used to treat breast cancer. Tamoxifen, letrozole, and anastrozole are a few of these. Tamoxifen appears to be helpful in a small proportion of patients with advanced ovarian cancer, according to preliminary trials. Letrozole may aid in ovarian cancer that is oestrogen receptor positive in slowing or stopping its growth. Anastrozole is being studied in postmenopausal patients with cancer that has the oestrogen receptor. There is also active research towards reducing the negative effects of ovarian cancer treatment.Hyperbaric oxygen therapy may provide relief from radiation fibrosis, the development of scar tissue in a radiation-treated area, but further research is needed in this area. Patients receiving treatment for ovarian cancer could also suffer.

6.**Inflammation**-There are some signs that pelvic inflammatory disease and ovarian cancer may be related, particularly in non-Western nations. It might be brought on by the pelvic inflammatory disease's inflammatory process.

7.**Clinical Studies**-Governmental entities in the US oversee and support clinical trials that test treatment options to determine whether they are secure and efficient. These include ClinicalTrials.gov, Learn About Clinical Trials, Search for Clinical Trials, NIH Clinical Research Trials and You, Learn About Clinical Trials, and the National Cancer Institute. Canada also conducts clinical trials.

Conclusion:

Incidence and mortality from cancer are primarily attributed to OC globally. The scope of the issue is discussed in this review, which also provides an overview of epidemiological research that revealed genetic, environmental, and lifestyle factors that may both raise and decrease the risk of this fatal disease. These elements undoubtedly have an impact on the various patterns and trends of OC incidence and death observed around the world. Reduced parity and changes in diet and physical activity may have something to do with the increasing trends seen in several countries with economic growth, while increased and earlier use of oral contraceptives has likely contributed to the declining trends seen in most developed countries.The majority of risk variables change significantly between the five histologic subtypes, particularly between the mucinous and non-mucinous subtypes, indicating different etiologies. Although such inference is limited, the fact that risk factor relationships support widely recognised models of pathogenesis for the specific histotypes lends support to causation. Mendelian randomization studies have inferred a likely causal relationship between BMI and risk of non-HGS OC and between vitamin D and risk of invasive and HGS OC. These studies rule out explanations such as bias, confounding, and reverse causality.When mistakes in ovarian cell development occur, ovarian cancer develops. Cells often die as they are old or injured, and new cells replace them. When damaged or ageing cells do not degrade as they should, cancer begins to grow. An ovarian tumour or growth is a lump of tissue that develops when there is an accumulation of excess cells. These cancer cells are genetically aberrant and develop uncontrollably as a result.The egg follicle ruptures and transforms into the corpus luteum when an ovary releases an egg. Cell division in the ovary is required to restore this structure. Long-term continuous ovulation necessitates more ovarian repair by dividing cells, which might result in mutations in individual cells.

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