Project Title

"Unheard Voices: Understanding the Needs and Experiences of Ovarian Cancer Patients"

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

Submitted By :

Nayema Najnin Riya
Batch: 23 (A)
Student Id: 201-29-1637
Department of Pharmacy
Daffodil International University..

March 2024

Approval

This project paper **"Unheard Voices: Understanding the Needs and Experiences of Ovarian Cancer Patients"** submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

Board of Examiners

……

Professor Dr. Muniruddin Ahmed

Professor & Head Department of Pharmacy

Faculty of Allied Health Sciences

Daffodil International University.

……	**Internal Examiner 1**
……	**Internal Examiner 2**
……	**External Examiner**

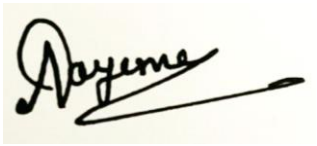
Declaration

I, at this moment, announce that I am carrying out this project study under the supervision of "Mr. Mohammad Touhidul Islam," Senior Lecturer, Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, Impartial Compliance with the Bachelor of Pharmacy Degree Requirement (B. Pharm). This project, I declare, is my original work. I also state that neither this project nor any part thereof has been submitted for the Bachelor's award or any degree elsewhere.

Supervised By:

Mr. Mohammad Touhidul Islam
Senior Lecturer
Department of Pharmacy
Faculty of Allied Health Sciences
Daffodil International University

Submitted By:



Nayema Najnin Riya
ID: 201-29-1637
Department of Pharmacy
Faculty of Allied Health Sciences
Daffodil International University

Acknowledgement

Firstly, I would like to express all my gratitude to Almighty Allah, who has granted me courage and the strength to complete this project.

A project is never the work of an individual. It is more than a combination of folk ideas, suggestion, reviews, contributions and work. A project's achievement and final outcome required a lot of guidance and support from many people, and I am extremely privileged to have acquired this all along until my paper is finished.

I feel obliged to take this opportunity to express my sincere thanks to Professor Dr. Muniruddin Ahmed, Head of Department of Pharmacy at Daffodil International University. My heartfelt thanks to my Supervisor Mr. Mohammad Touhidul Islam, Senior Lecturer, Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, who cared intensively for my project work and guide me throughout. I would like to express my heartfelt gratitude to my supervisor for allowing me to work under him, for his precious time in spite of his busy schedule, for his academic and administrative support and for the motivation and care as well.

Dedicated

To

My Parents and Supervisor...

Abstract

For women in particular, ovarian cancer is a serious health issue because of its poor prognosis, lack of a clear etiology, and frequent misdiagnosis. Furthermore, poor treatment tolerance and metastasis predispose individuals to recurrences. Using cutting-edge therapeutic methods in conjunction with tried-and-true strategies can help improve therapy results. Natural chemicals are particularly advantageous in this regard due to their multi-target effects, extensive use history, and general availability. Thus, the realm of organic and nature-derived goods may yield therapeutic options that are efficacious and increase patient tolerance. Furthermore, it is widely believed that natural substances have a smaller impact on healthy cells and tissues, indicating their potential use as effective substitutes for pharmaceuticals. These compounds' anticancer activities are often linked to decreased cell growth and metastasis, enhanced autophagy, and better chemotherapeutic response. This review attempts to address, from the standpoint of medicinal chemists, the molecular insights and potential targets of natural chemicals against ovarian cancer. A summary regarding the pharmacology of the organic compounds that have been investigated thus far in relation to their possible use with ovarian cancer forms is also provided. The existing bioactivity data and chemical features are examined and analyzed, with special focus on the molecular mechanism that underlies them or mechanisms. To understand the actual perception of the local people this survey was conducted from August 5 to November 10, 2023. A total of 200 ovarian cancer patients were interviewed the responder's average age was between 41-70 years 65%. 41-70 years old peoples are most prone to develop Ovarian Cancer. Above 70 years are also very risky in this scenario. The majority of respondents were having loss and also feeling tiredness. According to the respondent's, the majority of people is suffering from this problem for more than 1 year. Majority of people is suffering from this problem is thinking about surgery or going to surgery very soon. Almost half of the people who is getting treatment for cancer unsatisfied with the treatment they are getting for their diseases. The cost of higher for 69% of the people who is getting treatment for cancer and also it is hampering their family life. Only 13% of think that the treatment they are getting good enough for them but other 87% people are not happy with it.

Table of Contents

CHAPTER 1

INTRODUCTION

1. Introduction:

When bodily cells alter and proliferate uncontrollably, it results in cancer. Let's examine regular bodily functions to assist you better comprehend what happens to your body when you have cancer. The minuscule components of your body are known as cells. Normal cells proliferate when your body requires them and divide when that requirement is met. The aberrant cells that cause cancer proliferate even when your body doesn't require them [1]. The aberrant cells in most malignancies proliferate to create tumors, which are lumps or masses. Long-term presence of cancer cells in the body allows them to proliferate and infect neighboring tissues. They may even metastasize, or spread to different areas of the body [2]. Cancer that originates in the reproductive organs or at the tip of the fallopian tubes, which are located next to an ovary is known as ovarian cancer. This type of cancer only affects those who have ovaries. The ovaries can develop a variety of tumor forms. Some are safe. Thus, they are not cancerous. Benign tumors can become fairly large and present with symptoms, but they do not spread. Usually, one ovary or a portion of an ovary can be removed to cure them. Malignant, or cancerous, tumors include ovarian cancer. A malignant tumor has the potential to develop and grow to other body areas if left untreated [3]. The most deadly gynecologic malignancy is epithelial ovarian carcinoma. It ranks as the fifth most prevalent cancer within women in the US and is the fourth leading cause of cancer-related mortality in women, behind cancers that affect the lungs, breast, colon, & uterine. According to estimates from the National Cancer Institute and American Cancer Society, there would be 14,270 female deaths and 21,980 additional instances of ovarian cancer in 2014[4] . One in every 72 women, or 1.38% of all women, may get epithelial ovarian cancer throughout their lifetime. In addition, women who have a documented genetic susceptibility to this illness through family history are at much higher risk [5].

A class of illnesses known as ovarian cancer include those that start in the ovaries or in adjacent regions such the peritoneum and fallopian tubes. Each ovary on either side of the womb is housed in the pelvis of a female. The female hormones and eggs needed for reproduction are produced by the ovaries [6]. The two long, thin tubes on either side of the womb are known as fallopian tubes in women. The fallopian tubes carry eggs from the ovaries to the uterus. The tissue lining the abdominal organs is called the peritoneum. Treatment is most effective when cancer of the ovary is discovered in its early stages. It's critical that you pay close attention to the way you feel and understand what is typical for you because signs and symptoms of ovarian cancer are frequently present [7]. Visiting your physician, nurse, or other healthcare provider is the only method to

determine if your symptoms are related to cancer or something else. You may be more susceptible to ovarian cancer if you have certain genetic abnormalities [8]. The most frequent mutations that increase the risk of ovarian cancer are those linked to Lynch syndrome and the cancer risk genes 1, 2. There are several distinct tumor types & subtypes of ovarian cancer. Adenocarcinoma is the most prevalent tumor kind, and serous adenocarcinoma is the most prevalent subtype. Serious adenocarcinomas are primarily high-grade tumors, meaning they develop aggressively [9].

1.1 **Types of ovarian cancer**

1.1.1 **Epithelial ovarian carcinomas**

Most ovarian epithelial tumors are benign. On the other hand, the most prevalent kind of ovarian cancer is epithelial ovarian carcinoma, sometimes referred to as malignant epithelial tumors. The American Cancer Society states that the epithelial cells, that cover the ovary's outer surface, are the source of 85–90% of ovarian malignancies. While spreading to other areas of the body, such as the lungs and liver, they frequently affect the inner tissue and organs behind the pelvis and abdomen. Additionally, they could spread to the skin, bones, and brain 10].

Tumors of the epithelium that are malignant have several subtypes. The ones listed below are the most typical 52 percent of epithelial ovarian cancers are serous carcinomas, which are categorized as either high-grade or low-grade based on the appearance of the cancer cells in comparison to normal cells. A higher grade indicates that the cancer germs are proliferating quickly and may benefit most from treatment [11].

Endometrioid carcinomas: These have a propensity for sluggish growth and few symptoms. These tumors usually don't react as well to therapies, despite the possibility that they won't spread rapidly to other parts of the body [12].

Mucinous carcinomas: These usually afflict elderly women and make up 6% of instances of ovarian cancer. These slow-growing tumors are seldom identified in women under 35.When detected and treated in its early stages, clear cell carcinomas, a rare form of ovarian cancer, have a favorable prognosis [13].

Primary peritoneal carcinoma or fallopian tube cancer are two more cancer forms that resemble epithelial ovarian cancer. They are frequently treated using the same methods and strategies as

epithelial ovarian cancer because of their similar characteristics. The abdominal and pelvic linings are the sites of primary peritoneal carcinoma development. The fallopian tubes are the site of fallopian tube cancer. Both are uncommon [14].

1.1.2 Germ cell tumors

These start in the cells of reproduction, found in the sperm and eggs of men and women, respectively. According to the American Cancer Society, germ cell tumors account for less than a quarter of all ovarian malignancies and have a remarkable mortality rate, with 9 out of ten patients living five years following diagnosis [15].

The following are a few of the most typical subtypes of ovarian germ cell tumors:

Teratomas: These are germ cell tumors that can be either malignant (immature) or benign (mature), and their cells can include a variety of tissues, including bone, muscle, and hair. Rare are immature teratomas [16].

Dysgerminoma: The most prevalent ovarian cancer derived from germ cells, however uncommon [17]. Although dysgerminomas normally do not develop or spread fast, they have the potential to do so and can spread to other body areas, including the brain and spinal cord [18].

Chorionima tumors and endodermal sinus tumors (also known as yolk sac tumors): Endodermal sinus tumors usually affect children and originate in the female reproductive organs or testes [19]. Choriocarcinomas can originate in the ovaries and, more frequently, in the uterus during pregnancy. Both are quite uncommon. Ovarian cancer of this kind is more common in teenagers especially women in their 20s. Germ cell tumors usually affect one ovary, making it simpler to preserve a woman's fertility while undergoing therapy [20].

1.1.3 **Stromal cell tumors**

According to the ACS, ovarian stromal cell tumors, also known as sex cord tumors or sex cord-gonadal stromal tumors, are even less prevalent than ovarian germ cell tumors, accounting for only 1% of all ovarian malignancies. They arise from the progesterone and estrogen-producing stroma tissue cells in women [21].

Stromal tumors develop in the tissues supporting the ovaries in cases of ovarian cancer. Granulosa cell tumors make up the majority of the subtypes of malignant stromal tumors. Sertoli-Leydig cell tumors and granulosa-theca tumors are two other kinds. Early-stage detection is common for this kind of ovarian cancer. Vaginal bleeding is a frequently seen symptom. Among other hormonal signs, sudden vaginal bleeding should trigger a visit with a physician, especially for post-menopausal women [22].

1.1.4 **Ovarian sarcoma**

Opportunistic sarcoma tumors grow in the surrounding tissues of ovarian cells, in contrast to their carcinoma counterparts. When compared to other ovarian malignancies, it often has a poor prognosis and has not been well investigated. Pain in the abdomen is the most typical symptom [23].

Kruk Enberg tumors: Due to its metastatic character, which refers to the cells' easy separation from the initial tumor and rapid multiplication, Kruk Enberg tumors are regarded as stage 4 illness, or advanced cancer. Usually, this kind of tumor is located in the ovaries, colon, or stomach. This tumor may produce gastrointestinal symptoms, although it is usually asymptomatic [24].

Ovarian cysts: These form within the ovary and are sacs filled with fluid. They frequently disappear on themselves without medical intervention and are prevalent after ovulation. While majority ovarian cysts seem benign, some have the potential to become cancerous [25].

1.2 Signs and Symptoms

Ovarian cancer can manifest in a variety of ways. Even ovarian cancer in its early stages can generate symptoms, however women are prone to have them if the illness has progressed.
Among the most typical symptoms are:

- Bloating Pain in the abdomen or pelvis
- Difficulty eating or rapidly feeling satisfied
- Urinary symptoms include regularity (having to go constantly) or anxiousness (always thinking like you should go)

In addition to malignancies of other organs, benign (non-cancerous) illnesses are as frequently responsible for these symptoms [26]. They are often chronic and deviate from normal in nature

when they are brought on by ovarian cancer; for instance, they may occur more frequently or be more severe. Most of these symptoms are just as common in women without ovarian cancer, and they are more inclined to be brought on by other illnesses. However, consult your physician if you experience these symptoms at least once a month so that the issue may be identified and, if required, addressed [27].

Additional signs of ovarian cancer may consist of:

- Fatigue (severe exhaustion)
- Upset abdomen
- Back ache
- During-sex pain Constipation
- Variations in a woman's menstrual cycle, such as thicker or more erratic bleeding
- Swollen abdomen (belly) after losing weight [28].

1.3 Stages of Ovarian Cancer

The Memorial Sloan Kettering medical staff may create a personalized treatment plan for you based on the kind and stage of your ovarian cancer, which ranges from the youngest to the most advanced. Primary peritoneal cancer and fallopian tube cancer are frequently addressed with ovarian cancer in cancer education [29]. This is a result of the identical treatments given to all three of these malignancies. The route that eggs take from the reproductive organs to the uterus is provided by the fallopian tubes. The majority of the internal organs of the body, including the uterus, liver, & spleen, are located in the peritoneal cavity, which is the area of the abdomen. The lining inside this cavity is called the peritoneum [30]. Ovarian cancer can take many different forms, and it starts with these cell types:

- Surface epithelium, or the cells covering the lining of the ovaries
- The cells that will create eggs are called germ cells.
- The hormone-releasing cells known as stromal cells link the various ovaries' components.

Your MSK expert has to know the stage of ovarian cancer after a diagnosis in order to assess potential spread. In order to accomplish this, your surgeon is going to remove the tumor along

with tiny tissue samples from the peritoneum, fallopian tubes, and other internal organs in the abdomen. (Most of your digestive tract are found in your peritoneal cavity.) These samples are delivered to our lab so that one of our skilled pathologists may use a microscope and other instruments to check them for cancer cells [31].

The pathology reveal, which includes information on the type of cancer discovered, the dimension of the tumor, and whether the disease was confined within the ovary, will thereafter be sent to your MSK expert.

From early to late cancer, there are four phases of ovarian, fallopian tube, and peritoneal cancer [32].

Ovarian cancer at stage I is regarded as an early stage.

There are three sub stages within this stage, A, B, and C:

- Stage IA: a single ovary nor fallopian tube has cancer cells in it.
- Stage IB: Either ovaries or both fallopian tubes have cancer cells.
- Stage IC: either the ovaries or their fallopian tubes have cancer cells, along with one of the reasons that follow:

There are cancerous cells on the exterior of the ovaries either fallopian tubes; the capsule that surrounds the ovary has cracked apart; or Your peritoneal cavity, the tissue lining it, or the fluid coming from your abdomen can all contain cancer cells [33].

Cancer in stage II has started to spread. Two phases, A and B, comprise this stage:

- Stage IIA: cancer that has progressed from the fallopian tubes to the uterus and/or the ovaries, or via the ovary or ovaries to the uterus and/or the fallopian tubes.
- Stage IIB: The bladder, the intestines or rectum have been affected by cancer that began in your peritoneal cavity [34].

Cancer in stage III is further advanced. There are three sub stages within this stage, A, B, and C:

One of two definitions applies to Stage IIIA: The nearest lymph nodes, known as the retroperitoneal lymph nodes, are where cancer cells have spread. The pathologist may observe

that the malignant cells have traveled to the peritoneum (line) outside of the pelvis by looking at the samples under a microscope, something the surgeon is unable to see with the naked eye. There's a chance the malignancy has also moved to adjacent lymph nodes [35].

Stage IIIB: the surgeon can spot cancer within the peritoneum, but it is still no more than two millimeters. In addition, the cancer has progressed outside of the pelvis. There's a chance it reached adjacent lymph nodes [36].

The most advanced stage of ovarian cancer is called stage IV cancer.

A and B are the two sub stages:

- Stage IVA: excess fluid that has accumulated around the lungs contains cancer cells.
- Stage IVB: The disease has progressed to external organs and tissues, such as groin lymph nodes [37].

1.4 Diagnosis of ovarian cancer

Determining the reason of a health issue is an aspect of diagnosis. Going to a family doctor is typically the first step in the diagnosis of ovarian cancer. In addition to performing a physical examination, your doctor will inquire concerning any symptoms you may be experiencing. Your doctor may prescribe tests to screen out ovarian cancer or similar health issues based on this knowledge, or they may send you to a specialist [38].

Diagnosis procedures might appear laborious and irritating. While it's fair to be concerned, keep in mind that ovarian cancer symptoms can also be caused by other medical disorders. Before diagnosing ovarian cancer, the medical team must rule out other possible causes of the health issue [39].

Typically, ovarian cancer is diagnosed or ruled out using the tests listed below. The stage—or the extent to which the cancer has progressed—is determined by many of the same tests that are used to identify the disease. In order to assess your overall health and assist in treatment planning, your doctor could possibly prescribe further tests [40].

Medical history and examination

Your prior medical occurrences and issues, along with your symptoms and risk factors, are all documented in your health history. Your physician will inquire about your past experiences with:

Signs and symptoms of ovarian cancer

- Mammary cancer
- Hereditary non-polyposis cancer of the colorectal, or HNPCC, is another name for Lynch syndrome.
- Gestations
- Replacement hormone treatment
- Asbestos exposure from smoking
- A family tradition of: may also be inquired about by your doctor.
- Breast or ovarian cancer
- Infertility warning signs for ovarian cancer as well as other malignancies, including breast, uterine, and colorectal cancers, are associated with Lynch syndrome, also known as hereditary non-polyposis cancer of the colorectal, or HNPCC [41].

Sonography

An ultrasound creates pictures of bodily components by using high-frequency sound waves. To check for ovarian cancer, a transvaginal or pelvic ultrasound may be performed. Instead of putting the ultrasound probe on the outer layer of the abdomen, the transvaginal ultrasound technique places it into the vagina and directs it toward the ovaries [42]. Using ultrasounds, one can: locate an ovarian tumor and determine if it is a cyst filled with fluid or a solid tumor. Observe the ovary's size, shape, and inside appearance. Assess any anomalies in the pelvic organs other than the kidneys look for any fluid accumulation in the abdomen [43].

Testing for tumor markers

Substances discovered in the blood, tissues, or bodily fluids after removal are known as tumor markers. Tests for tumor markers are often used to monitor for recurrences and assess how well you are responding to cancer therapy. They can be useful in the diagnosis of ovarian cancer as well [44].

For ovarian cancer, the following tumor markers can be evaluated.

- Women with benign diseases, various malignancies, and ovarian cancer may have greater levels of cancer antigen 125 (CA125).
- Women who have benign diseases other than ovarian cancer may have greater levels of carcinoembryonic antigen (CEA).
- Younger women with ovarian germ cell tumors may have greater levels of a hormone called human chorionic gonadotropin (HCG or b-HCG).
- The levels of alpha-fetoprotein (AFP) in younger women with ovary germ cell tumors could be elevated [45].

Total blood count (TCB)

White blood cell, red blood cell, and platelet counts are measured by a complete blood count (CBC). A complete blood count (CBC) is performed to assess your overall health and look for anemia from chronic bleeding into the vagina and to offer a standard against which subsequent CBCs during and following therapy can be compared [46].

Tests for blood chemistry

Tests for blood chemistry quantify certain substances in the blood. They can assist in identifying anomalies and demonstrate how effectively a certain organ is operating. It is possible to assess lactate dehydrogenase (LDH) in female ovarian cancer patients. Elevated levels could suggest a tumor of the ovarian germ cell. Several women having ovarian stromal tumors may have higher-than-normal amounts of hormones such estrogen, testosterone, and inhibin [47].

CT scan.

Using specialized x-ray equipment, a computed tomography, or CT, scan creates cross-sectional and three-dimensional pictures of the body's organs, tissues, bones, and blood arteries. The photographs are converted into detailed visuals by a computer.

Using a CT scan, you can:

Examine the abdomen, pelvis, and the lymph nodes within the ovaries.to see if the cancer has progressed to other tissues or organs. Direct the needle when performing a biopsy in a suspected metastatic region [48].

An MRI

Strong magnetic fields and radiofrequency waves are used in MRI, or magnetic resonance imaging, to create cross-sectional pictures of bones, tissues, organs, and blood vessels. Three-dimensional graphics are created by a computer.

Using an MRI, one can:

Examine the abdomen, pelvis, and the lymph nodes within the ovaries.to see if the cancer has progressed to other tissues or organs. Direct the needle when performing a biopsy in a suspected metastatic region [49].

An endoscopy

A tiny incision is made in the belly by the doctor during a laparoscopy, and a thin tube known as a laparoscope is inserted inside the abdominal cavity. Small tissue fragments can be removed using surgical tools inserted through the laparoscope. One uses a laparoscopy to: remove tiny tumors or cysts; examine the abdomen for abnormal growths; get tissue samples via the ovaries along with other organs; assist in determining the cancer's stage; and arrange surgery or other therapies [50].

Autopsy

A biopsy involves the removal of bodily tissues or cells by the physician in order to examine them in a laboratory. The pathologist's report will indicate whether or not the sample contains cancerous cells. When doing biopsies for ovarian cancer, a laparotomy is frequently required. Ovarian cancer is diagnosed, staged, and treated with this operation, frequently concurrently [51]. To check every organ in the abdominal cavity, the surgeon creates a wide incision in the belly. The surgeon often removes the whole tumor during this procedure in addition to taking tissue samples from various abdominal and pelvic regions to check for potential metastases. To assist, the samples are submitted to the lab [52].

Ankyloglossia

A hollow needle and tube is introduced under the skin to enter the abdominal cavity during a paracentesis treatment. The purpose of this treatment is to remove the ascites, or symptomatic

accumulation of fluid within the lining of the abdomen. Cancer cells are screened for in the fluid [53].

A chest x-ray

Tiny radiation doses are used in x-rays to create images of bodily components on film. It is employed to search for indications of fluid surrounding the lungs (pleural effusion), which may be brought on by ovarian cancer that has progressed to the lungs [54].

Endoscopy

To rule off colon cancer or determine whether ovarian cancer has progressed to the colon, a colonoscopy can be performed [55].

PET scan.

Radiopharmaceuticals are radioactive substances that are used in PET (positron emission tomography) scans to detect modifications to the metabolic processes of bodily tissues. After analyzing the radioactive patterns, a computer creates color, three-dimensional representations of the region being scanned. If ovarian cancer has returned or spread to different organs or tissues, it may be detected using a PET scan [56].

1.5 Pathophysiology of Ovarian Cancer

The majority of ovarian malignancies are epithelial in origin, with a smaller number arising from the other cell types, including germ cell, mixed cell-type tumors, and sex-cord stromal.

- The most prevalent histological subtypes of ovarian carcinomas on epithelium are mixed (6%), mucinous (3%), transitional (1%), clear cell (12–13%), endometriosis (9–11%), and severe (68–71%).
- It has now been conclusively demonstrated by a number of organizations that epithelial ovarian cancer comes in two separate forms: type I and type II [57].
- Low-grade serous carcinoma, endometriosis carcinoma, and clear-cell carcinoma are examples of type I tumors that develop through a well-established process from either borderline serious tumors or from endometriosis.

- The majority of the time, these tumors are low-grade, early-stage diseases that progress slowly [58].
- Type II cancers are more common, often have a serious histology, are high grade, and in as many as 60% of cases, they appear to start in the fibril epithelium.
- At the time of diagnosis, the majority of ovarian epithelial cancers are advanced-stage, high-grade, serous carcinomas with a poor prognosis when compared to early-stage carcinomas. • Afterwards, high-grade serous carcinomas manifest clinically as stage 3 or 4 disease, in line with the hypothesis of peritoneal seeding by malignant cells from the fimbriae end of the tubes [59].

1.6 Controlling ovarian cancer

As existing approaches prove ineffective, further study into the identification, management, and treatment of ovarian cancer is required.

In particular, ovarian cancer arises from the proliferation of malignant cells on the ovary's surface, which then migrate or exfoliate into the peritoneal cavity and adhere to tissues like the momentum. Early-stage momentum tumors in women do not exhibit any particular symptoms, therefore the tumors go undiagnosed until they have grown significantly. Current approaches do not allow for the early identification the mutant cells in samples of serum because ovarian tumor cells cannot propagate into the bloodstream. It is necessary to develop more precise indicators and sensitive diagnostics for ovarian cancer [60].

The cytotoxic medications paclitaxel and cisplatin, which disrupt microtubule processes that govern cell division and block factors that regulate DNA repair, are being used to treat ovarian cancer. In addition to experiencing cytotoxic stress, which ultimately results in cell death, tumor cells also avoid cell death by proliferating into distinct daughter cells that are resistant to the toxic stress. These particular tumor cells, referred to as polyploidy gigantic cancer cells (PGCCs), give birth to daughter cells who develop resistance to stress and cytotoxic medicines due to changes in their DNA [61].

New detecting targets

While ovarian cancer cells can, but rarely do, spread to the breast and other organs, the majority of ovarian cancer tissue stays in the peritoneal cavity. While PAX8 is being used to detect ovarian

cancer cells that have spread, it lacks specificity. According to a recent study, SOX17 is a more specific protein than PAX8 and is expressed more selectively and at greater amounts in cancerous ovarian tissue along with metastatic locations [62].

Which are these variables

DNA Binding transcription element PAX8 (Paired BOX 8) has been utilized to detect initial tumor cells of many sources, including breast, adrenal, and ovarian cancers. As a result, tissue specificity is lacking. Nuclear protein SOX17, also known as SRY-box transcription factor, plays a key role in controlling genes involved in the development of several organs throughout embryogenesis. According to recent research, it is also significantly expressed in some esophageal carcinoma of squamous cell (ESCC) cells which are susceptible to cytotoxic treatments and high-grade secretory ovarian cancer (HGSOC) cells.

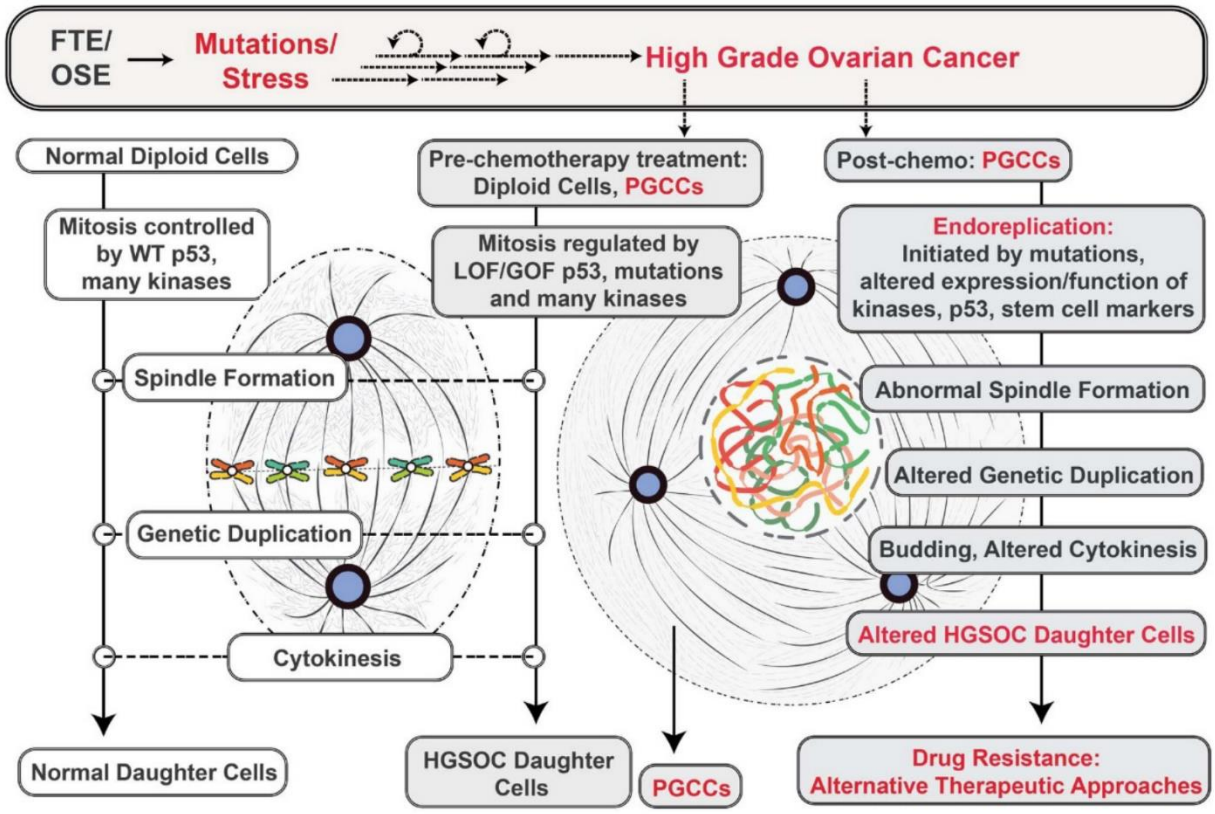


Fig 1: Ovarian cancer can develop from fallopian tube epithelial (FTE) [63]

Why is SOX17 USED?

According to a recent study, excessive SOX17 expression prevents several genes involved in tissue homeostasis and DNA repair from transcriptionally activating. BRCA1, BRCA2, RAD51, SIRT1, and p21CIP1 are some of these genes. Through inhibiting DNA repair, SOX17 makes these tissues more susceptible to anti-cancer medications like paclitaxel and cisplatin, which are meant to stop cancer cells from proliferating and cause them to die. On the other hand, significant levels of genes that repair DNA with resistance to agents that induce DNA damage are made possible by SOX17 methylation [64].

Breast cancer, SOX17, and PAX8

In addition to giving cisplatin and paclitaxel, routine therapy for ovarian cancer involves physically removing tumor tissue within the peritoneal cavity.

According to recent research, high levels of SOX17 and PAX8 are expressed by ovarian cancer, serving as two indicators of high-grade epithelial ovarian cancer. This contributes to the understanding of why cytotoxic medications are used in the treatment of ovarian cancer and why high-grade ovarian cancer is sensitive to them. Understanding one of the underlying processes by which ovarian cancer is mediatedly sensitive to particular medications is made possible by the recent characterization of SOX17 activity in ovarian cancer [65]. Treatments with cytotoxic drugs, however, do not completely eradicate cancer cells and the development of tumors. Recent research has revealed that 37–50% of high-grade cancers include PGCCs, which are special in their ability to resist cytotoxic stress. In particular, these cancer cells engage a special type of cell division called end replication when they experience stress. This mechanism ultimately produces a large number of daughter cells that are sensitive to the cytotoxic medications due to genomic rearrangements. PGCCs four [66].

What measures may be taken to prevent ovarian cancer?

Recent research confirms that SOX17 constitutes a crucial and highly specific ovarian cancer marker (2). As a result, it may prove to be a very helpful ovarian cancer predictor when combined with other tests to detect the existence of metastasis ovarian cancer tissue as well as to detect and confirm the early detection of malignant ovarian cancer (and a particular type of ESCCs) [67].The origins and pivotal function of PGCCs in the advancement of ovarian cancer are being increasingly highlighted by several recent investigations. Numerous distinct cytotoxic therapies employed in

tumor prevention have the potential to produce PGCCs. These include senescence brought on by viral oncogenes, hypoxia, chemotherapy, and radiation [68].

Consequently, in order to comprehend end replication—the process by which PGCCs endure and give rise to daughter cells that are resistant to drugs—we must comprehend the underlying molecular processes that govern it. With this information, fresh strategies for ovarian cancer management may be created. Notably, PGCC end replication is a very basic biological activity since it resembles the mechanism that takes place in early embryogenesis [69].

1.7 Treatment of Ovarian Cancer

The course of ovarian cancer treatment will depend on: The extent and kind of your ovarian cancer, its location, and if it has traveled to other parts of your body Chemotherapy and surgery are the primary therapies. Hormone therapies and certain medications are examples of further treatments. The specialized medical staff taking care of you will:

- Elucidate the side effects, advantages,
- And therapies.
- Collaborate with you to develop the best possible treatment plan discuss potential side effects and other aspects of the therapy with you

You will have routine examinations prior to and following any treatments. Also possible are scans and testing [70].

Operation

The kind of your cancer and its spread will determine the kind of surgery you need. Early diagnosis improves the prognosis for ovarian cancer patients. You could undergo surgery to remove the following if the cancer is still in its initial stages and has not progressed beyond of your ovaries:

The opening to the uterus from the inside of your vagina (cervix) plus your own womb (abdominal hysterectomy) both the ovaries and their fallopian tubes (both sides of salpingo-oophorectomy) You may require further surgery to remove as much of the cancer as possible if it has progressed to other regions of your body. A portion of the colon may be removed during this procedure [71].

Chemo medicine

One medication that destroys cancer cells is chemotherapy. It can be taken on its own or administered both before and after surgery. The treatment may also be applied to ovarian cancer that's returned [72].

Radiation therapy

High-energy radiation beams are used in radiotherapy to destroy cancer cells. For ovarian cancer, you could get radiation treatment to:

Handle advanced cancer if alternative therapies aren't appropriate for you assist with symptoms including bleeding, pain, or discomfort [73].

Targeted treatments

Targeted treatments are medications that specifically target molecules that aid in the growth or survival of cancer cells.

For advanced cancer of the ovary that has returned, they can be a possibility [74].

Hormone treatment

Estrogen is necessary for the development of some ovarian malignancies. Certain malignancies can be prevented from spreading by hormone therapy that restrict the synthesis of estrogen. Seldom are these medications utilized. If hormone therapy is appropriate for you, your doctor will advise you on how to monitor for and manage any adverse effects [75].

CHAPTER 2

PURPOSE OF THE STUDY

2. Purpose of the study

- To find out the present scenario of Ovarian Cancer patients in Bangladesh.
- To find out the reasons of Ovarian Cancer in the peoples of Bangladesh.
- To increases the awareness among the people of Bangladesh about Ovarian Cancer and its common reasons.
- To find out the present situation to understand the main reason of Ovarian Cancer.
- To help in the management of Ovarian Cancer patients life and how to get relief from it.
- To understand the future scenario of Ovarian Cancer and make people aware about this problem.

This study aims to understand the present, future and also the relief pattern of Ovarian Cancer patient and make an outcome of reasons of their problem for which reason they are suffering from Ovarian Cancer and other people aware about this reasons.

CHAPTER 3

LITERATURE REVIEW

3. **Literature review**

Current Approaches and Challenges in Managing and Monitoring Treatment Response in Ovarian Cancer

Abstract

Among gynecologic cancers, epithelial ovarian carcinoma is the most common cause of mortality. The management of persistent ovarian cancer is still difficult, even with improvements in surgical and chemotherapy techniques. Although there is disagreement about whether this affects the result, many doctors want to identify recurrences as soon as possible and start treatment. Several months may pass before recurrent symptoms manifest due to increases in CA125 and radiographic abnormalities. Even though it is uncommon to find recurrences alone by physical examination, a comprehensive exam combined with complaints of symptoms and increased CA125 can find 80–90% of recurrences. When there is a CA125 increase but no symptoms, a spiral CT scan can be performed to confirm recurrence; if the results of the CT scan are unclear, a PET/CT scan can provide more information. Chemotherapy administered before symptoms appear, even in the presence of increased CA125, had little effect on overall survival. This is mainly due to the low effectiveness of existing therapies in the recurrent situation. It is necessary to learn more about the biology of tumors and how to identify the people who will benefit from the various treatment approaches. As a result, the strategy for post-treatment surveillance ought to be customized when considering the therapeutic advantage of the second-line therapy in comparison to the expenses and side effects of the surveillance technique [76].

Updates and New Options in Advanced Epithelial Ovarian Cancer Treatment

Abstract

Treatment plans for women having epithelial ovarian cancer are still being developed, both medically and surgically. There has been notable advancement over the last few years, supported by important clinical studies. Even while systemic treatment and surgery are still used to treat

primary epithelial ovarian cancer, more sophisticated surgical techniques and cutting-edge medications are now considered standard of care. While maximal surgical effort and cytotoxic chemotherapy are still the gold standards, new research has raised doubts about the benefit of surgery for women who recurrent illness and tailored medicines are becoming more common. Poly ADP-ribose polymerase antagonists are being used more often because they have been shown to enhance progression-free prognosis in both frontline and recurrent situations. The suggestion that all women suffering epithelial ovarian cancer undergo germline genetic testing is reinforced by the recent establishment of therapy categories that depend on genetic alterations, and new biomarker-driven therapeutic approvals suggest that women may also benefit via somatic molecular testing. Enrollment in clinical trials, however, continues to be crucial for the discovery of new approaches. We believe that with the increasing body of knowledge regarding surgical techniques, targeted therapies like poly ADP-ribose polymerase blocks and antiangiogenics, and the novel therapeutic agents and mixtures under development, progressed epithelial ovarian cancer is going to cease to be an almost 100% fatal disease and become increasingly curable [77].

Effect of Surgeon Specialty on Processes of Care and Outcomes for Ovarian Cancer Patients

Abstract

Specialized care, or treatment provided by a specialist, has been linked to higher-quality care for several disorders (i.e., better results). We looked at correlations between the specialization of the doctor and the results in an aged population-based cohort of patients who underwent ovarian cancer surgery. Methods: Living in an area under the surveillance of the Surveillance, Epidemiology, as well as End Results (SEER) program, we analyzed the Medicare claims, broken down by physician specialty, of all women 65 years of age or older who underwent surgery over pathologically verified invasive epithelial ovarian cancer among January 1, 1992, and December 31, 1999. Our goal was to evaluate key care processes, such as the appropriate extent of surgery and the use of adjuvant chemotherapy, as well as outcomes, such as surgical complications, ostomy rates, while survival. Each and every statistical test has two sides. Findings: Of the 3067 individuals with ovarian cancer who underwent surgery; gynecologic oncologists treated 1017 patients (33%), general gynecologists handled 1377 patients (45%), and general surgeons treated 673 patients (22%). Patients managed either a gynecologic pathologist (60%) had a higher likelihood of undergoing lymph node dissection among those with stage I or II illness than were

patients treated by general gynecologists (36%) or general surgeons (16%). In patients who had stage III or IV disease, gynecologic oncologists were more likely to perform a debunking procedure (58%) than general gynecologists (51%) or general surgeons (40%; P <.001), and they were also more probable to administer postoperative chemotherapy (79%) or general gynecologists (76%) than general surgeons. Patient survival was higher between those operated on by generalist physicians (hazard ratio = 0.86, with a 95% CI = 0.78 to 0.96) and gynecologic therapists (hazard proportion [HR] of mortality via any reason = 0.85, 95% credible range [CI] = 0.76 to 19.5). Results: Patients with ovarian cancer treated as gynecologic oncologists had noticeably better results when compared to patients treated by general gynecologists, and significantly better results when compared to patients managed by general surgeons [78].

CHAPTER 4

METHODOLOGY

4. Methodology

4.1 Methods

This segment will provide an examination of the technique and strategy that will be employed to gather the data for the survey. This survey sought to ascertain the current, prospective, and pattern of relief for ovarian cancer. This section is of the utmost importance as it analyzes the approach to the survey along with methods that will be implemented to collect the survey's data.

4.2 Study design

Between August 5 to the 10th of November 2023, this in-person, questionnaire-based investigation involving ovarian cancer sufferers residing in rural as well as urban regions was conducted. I gathered the information for this investigation in person. To assure the reliability and authenticity of the data, it is necessary to develop a positive rapport with the participants. Prior to the meeting, the members were provided with an overview of the review's key arguments and objectives. A prudent strategy was implemented in managing, resuming, and resolving the acquired information.

4.3 Content of the survey

The researcher developed the structured questionnaires subsequent to an extensive review of prior research from scholarly databases, online journals, newspapers, online journals, and Google searches. The selection of these sources was predicated on necessity. Eight to ten minutes were required to respond to the fourteen closed-ended inquiries in the review. There is approximately 200 interest in this. A tangible sample for this research was collected from various specialized kidney institutions located in Bangladesh. The survey comprises various elements, namely: (1) socioeconomic data encompassing welcome, birthday, age, occupation social standing, and preceding health information; and (2) an assessment of the adult populace of Bangladesh's comprehension regarding cancer related conditions and the primary etiological factors associated with such ailments. For one month, two hundred individuals participated and responded to the survey.

4.4 Inclusion criteria

To be eligible, respondents were required to have been ovarian cancer patients residing in any region of Bangladesh.

4.5 Exclusion criteria

The exclusion criteria for the study stipulated that minors were not permitted to participate and that people who were not prepared to engage were also excluded.

4.6 Data Analysis

The complete survey data was inputted into the Microsoft Excel spreadsheet. Each issue has been specifically nurtured. The inventions are displayed alongside various factors that are proportional, relative, and percentage-based on the cultivation and attitude towards information.

CHAPTER 5

RESULT AND DISCUSSION

5 Result and discussion

5.1 Result

5.1.1 General characteristic of respondent:

Age

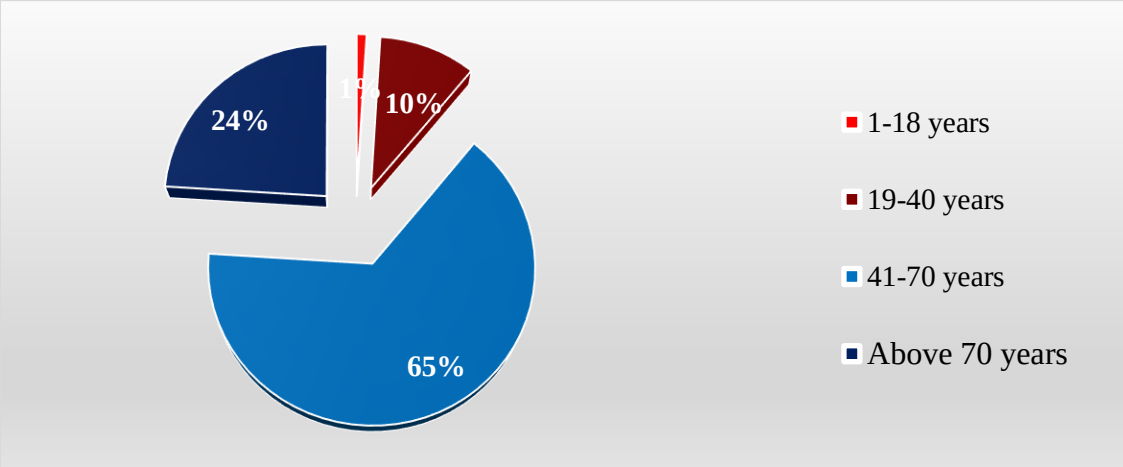


Figure 2: Age

The responder's average age was between 41-70 years 65%. 41-70 years old peoples are most prone to develop Ovarian Cancer. Above 70 years are also very risky in this scenario. As the age increases the chance of developing Ovarian Cancer increases.

Residence

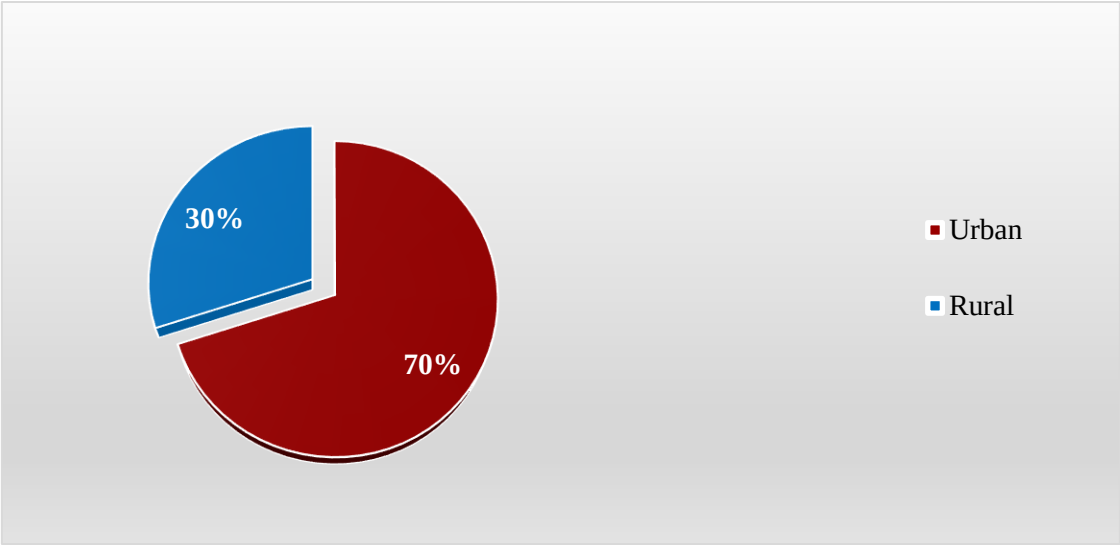


Figure 3: Residence ratio

The majority of respondents lived in rural areas (58%), Followed by urban areas (42%)

Occupation

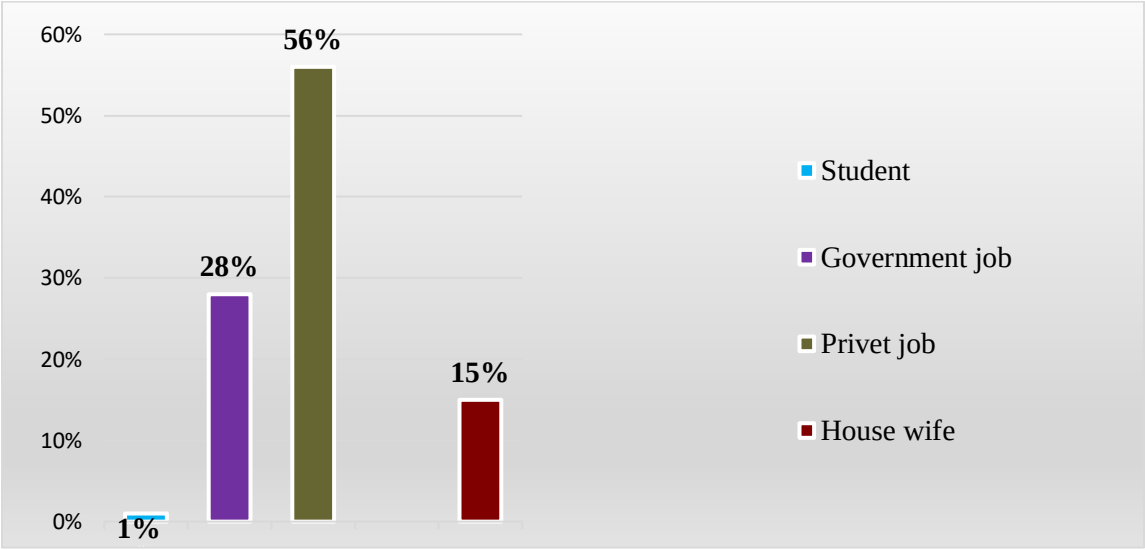


Figure 4: Respondents Occupation

According to the survey, the majority of respondents were privet job holders (56%).

5.1.2 Questionnaire about lifestyle changes and problems

What kind of problems faced before cancer detection

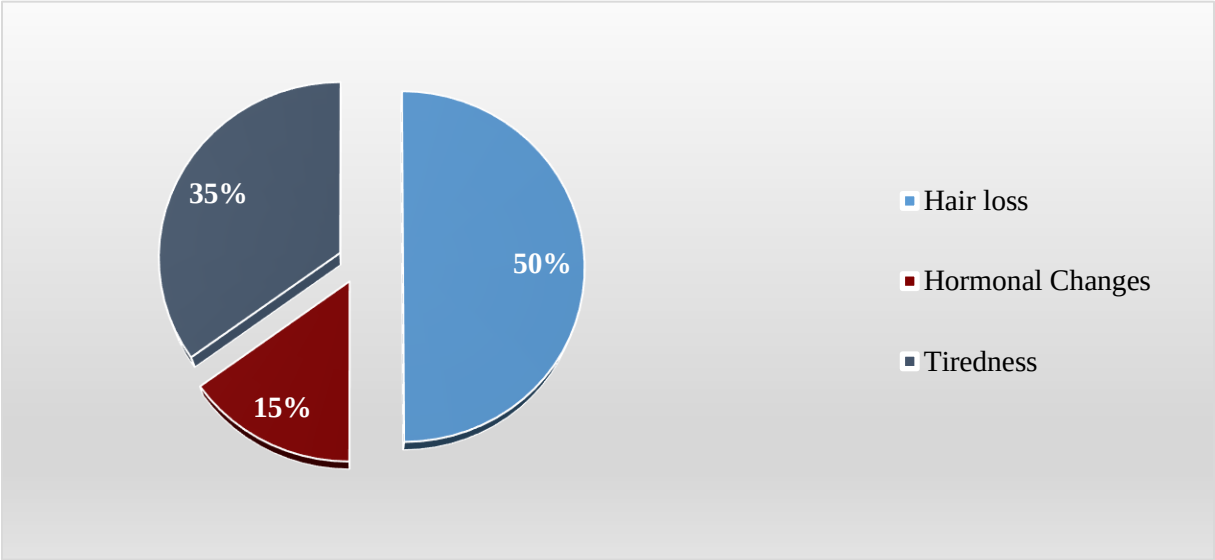


Figure 5: Problems faced

According to the survey, the majority of respondents were having loss and also feeling tiredness.

Bloating, diarrhea and abdominal pain did you knew about this problems

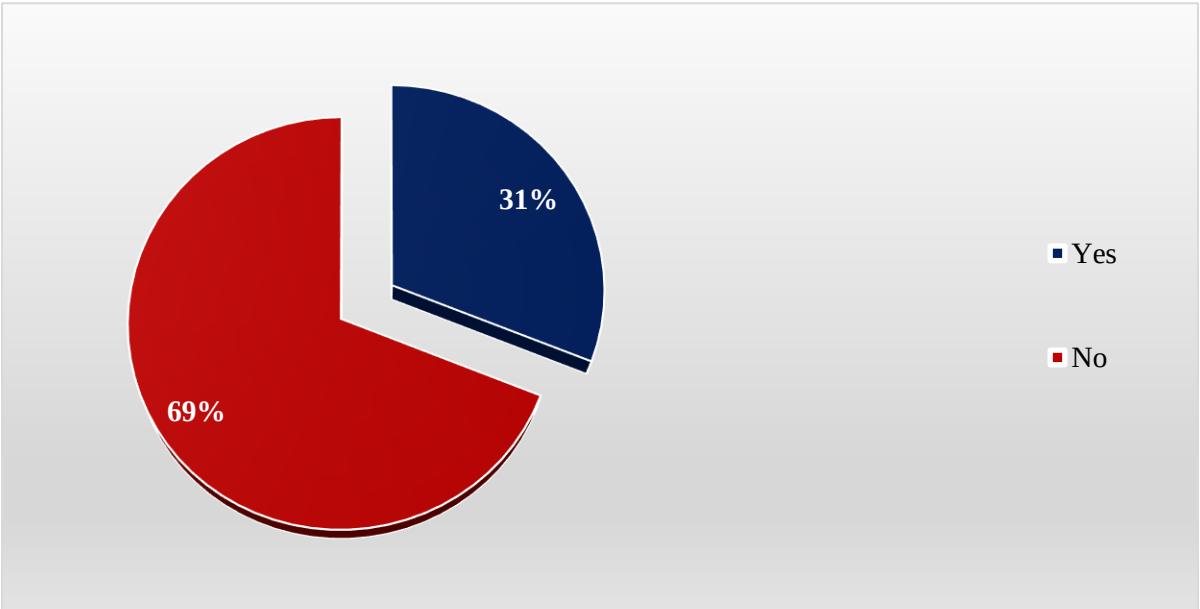


Figure 6: Knew about symptoms

The majority of respondents didn't knew about this symptoms approx. 69%.

Acid reflux, a dull ache or a feeling of pressure did you feel any of this?

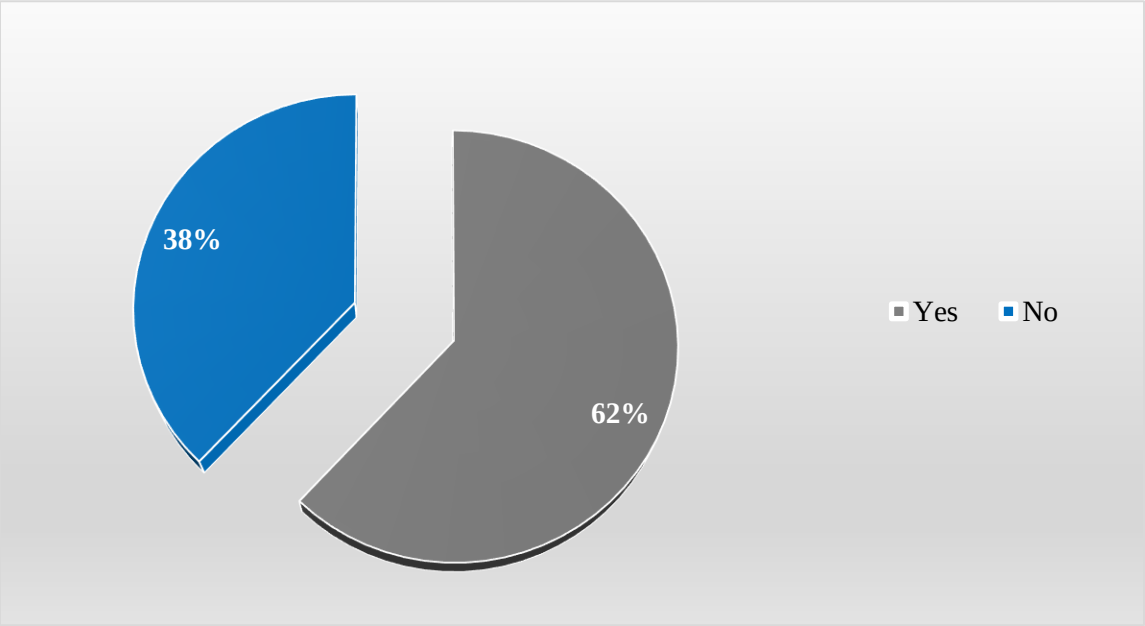


Figure 7: Different Feelings

According to the survey, the majority of respondents were having problems during this diseases.

5.1.3 Questionnaire about treatment and management

How long are you suffering from Ovarian Cancer?

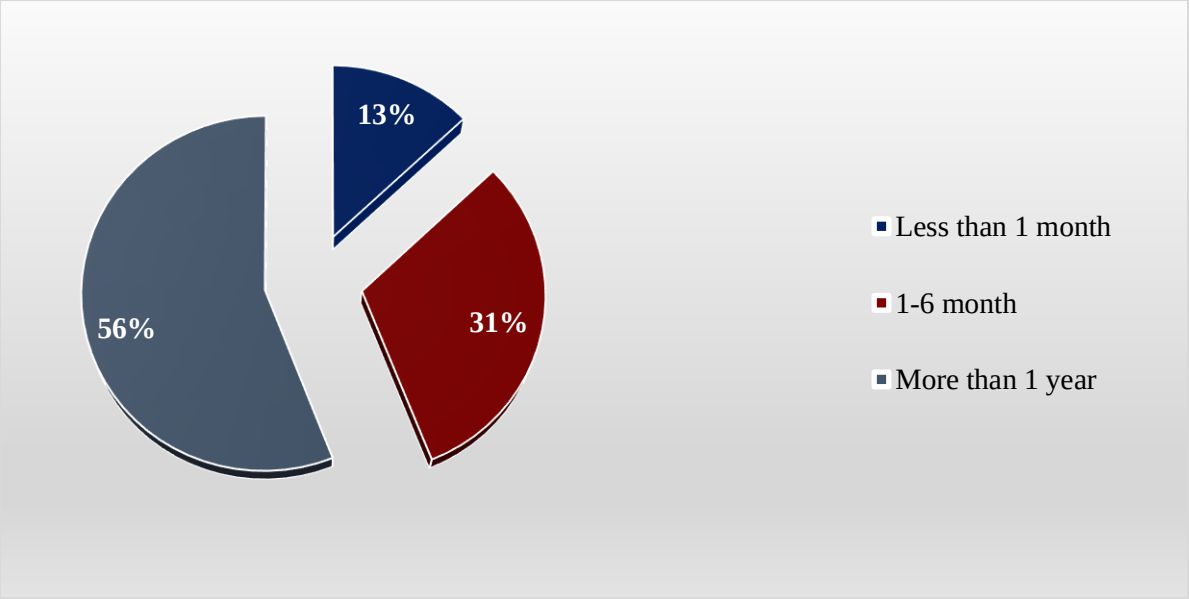


Figure 8: Suffering time

According to the respondent's, the majority of people is suffering from this problem for more than 1 year.

Which stage of Ovarian Cancer you are in right now?

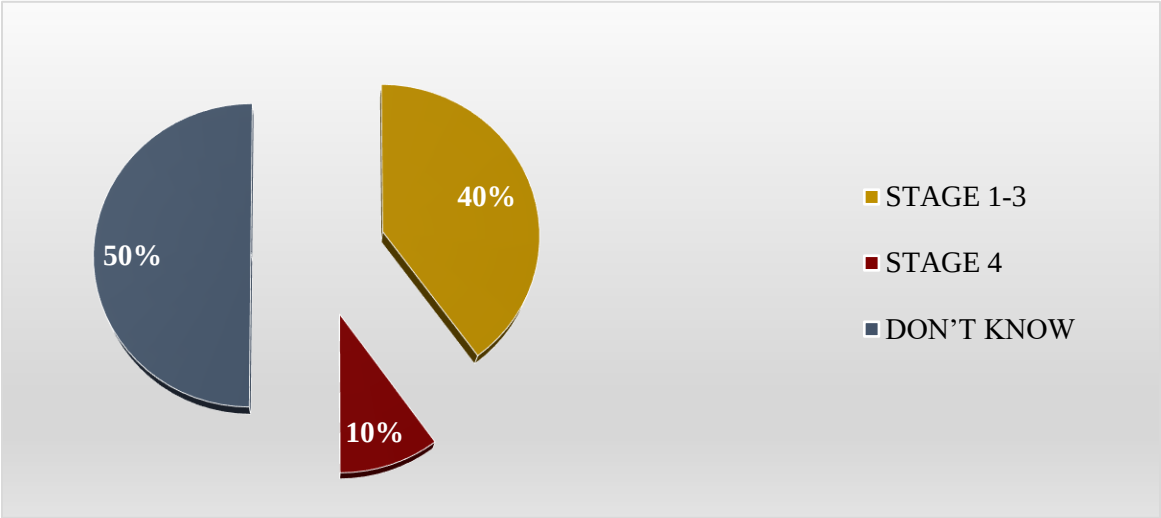


Figure 9: Stage of Cancer

The majority of respondents didn't knew about the stage they are in at that moment.

What type of treatment are you getting for your diseases?

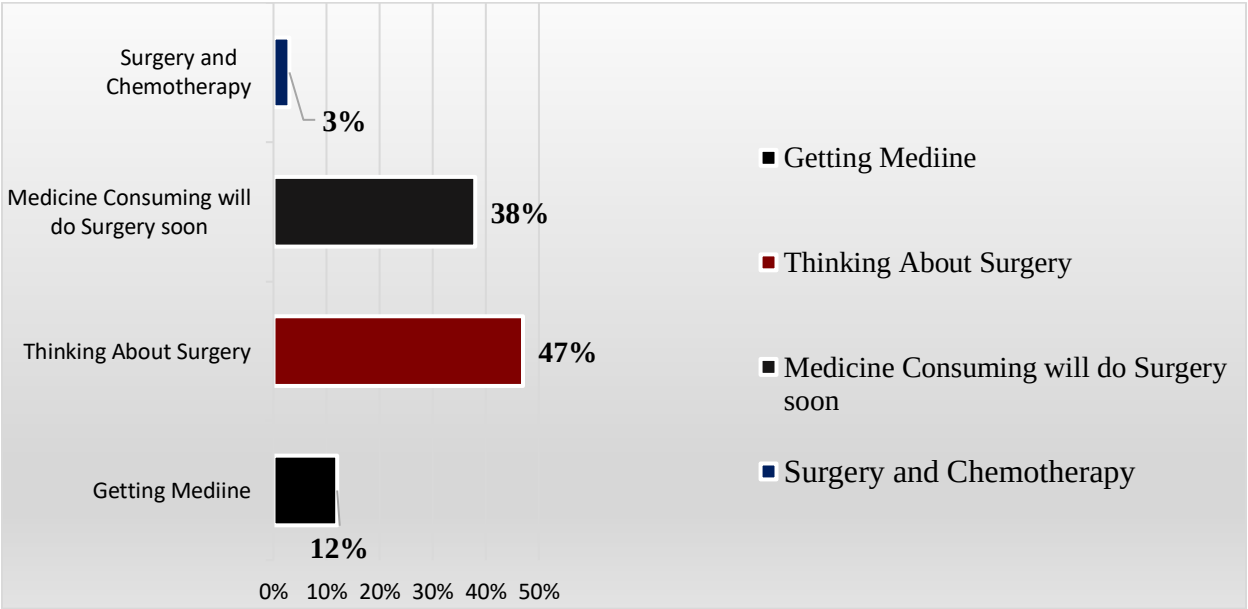


Figure 10: Treatment for Ovarian Cancer

According to the respondent's, the majority of people is suffering from this problem is thinking about surgery or going to surgery very soon.

Test done for the detection of Ovarian Cancer?

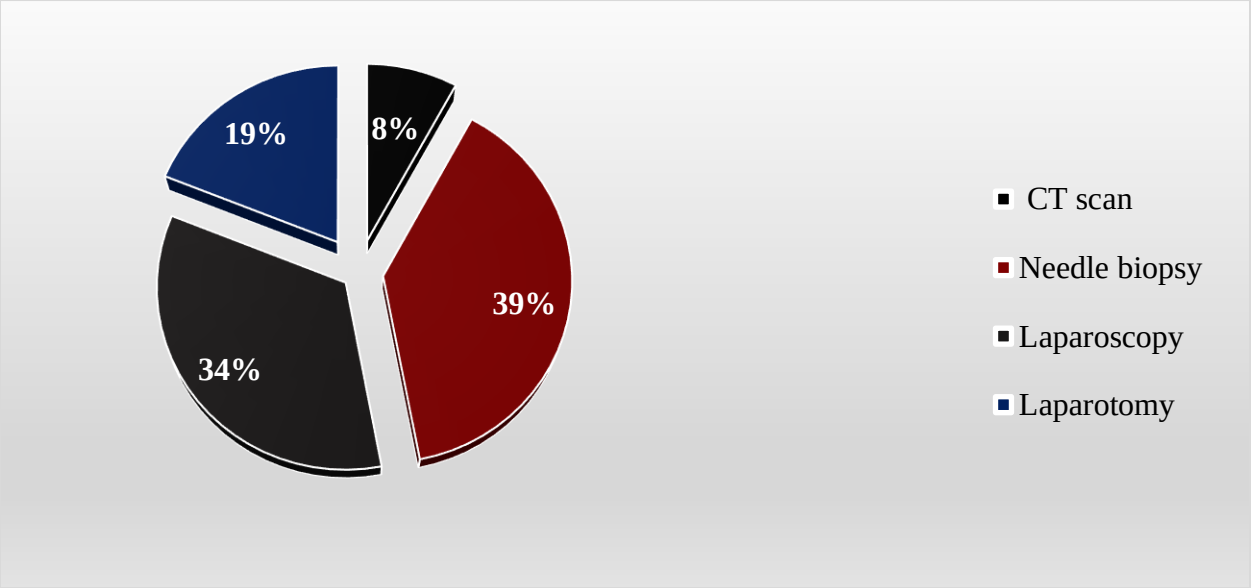


Figure 11: Detection test

The majority of respondents have done needle biopsy and laparoscopy for the detection of Ovarian Cancer.

Satisfaction about the treatment

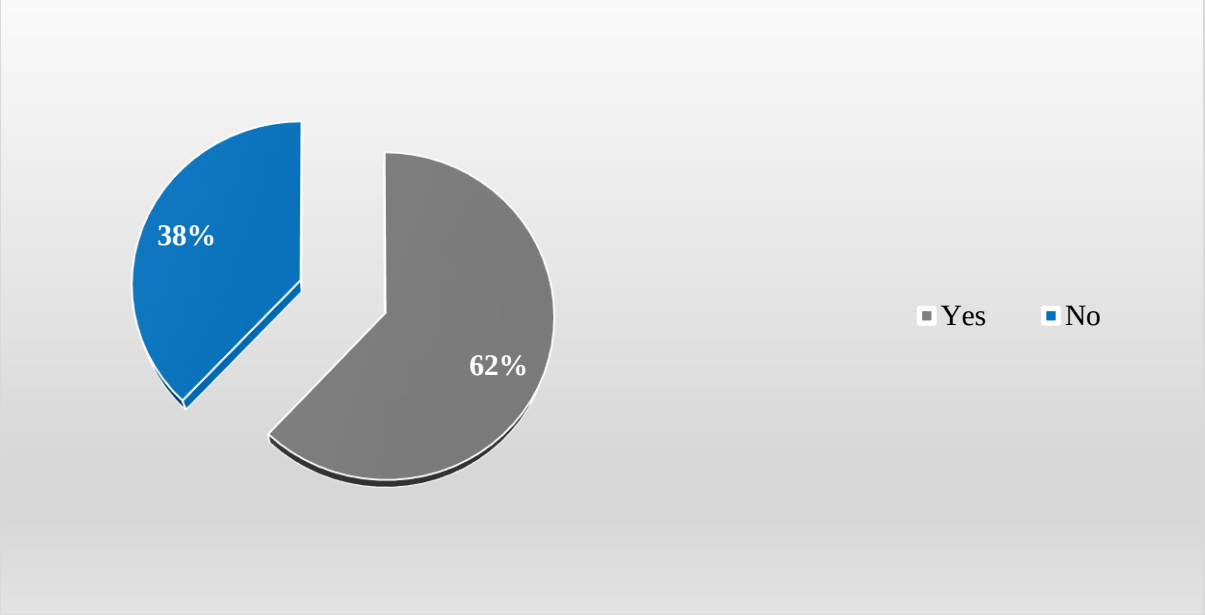


Figure 12: Satisfaction ratio

The people getting treatment for Ovarian Cancer almost 62% of the respondents are satisfied with the treatment they are getting.

What do you think about the present treatment scenario for cancer patients in Bangladesh?

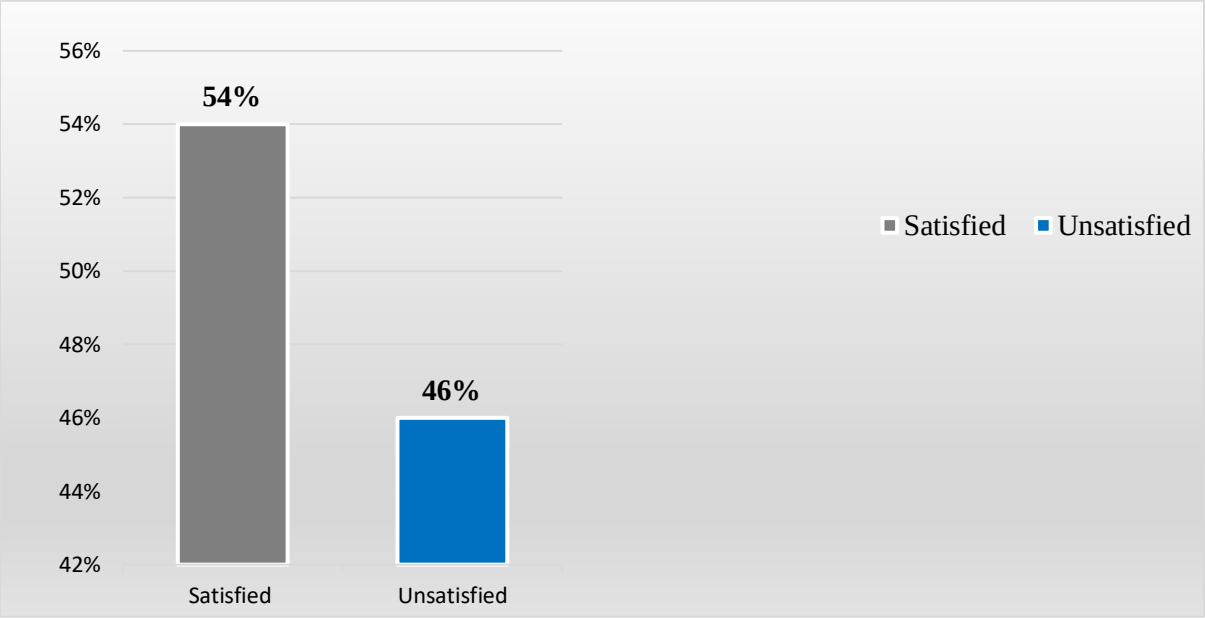


Figure 13: Present treatment scenario for cancer patients

Almost half of the people who is getting treatment for cancer unsatisfied with the treatment they are getting for their diseases.

The cost of the treatment is it normal for the all the patients?

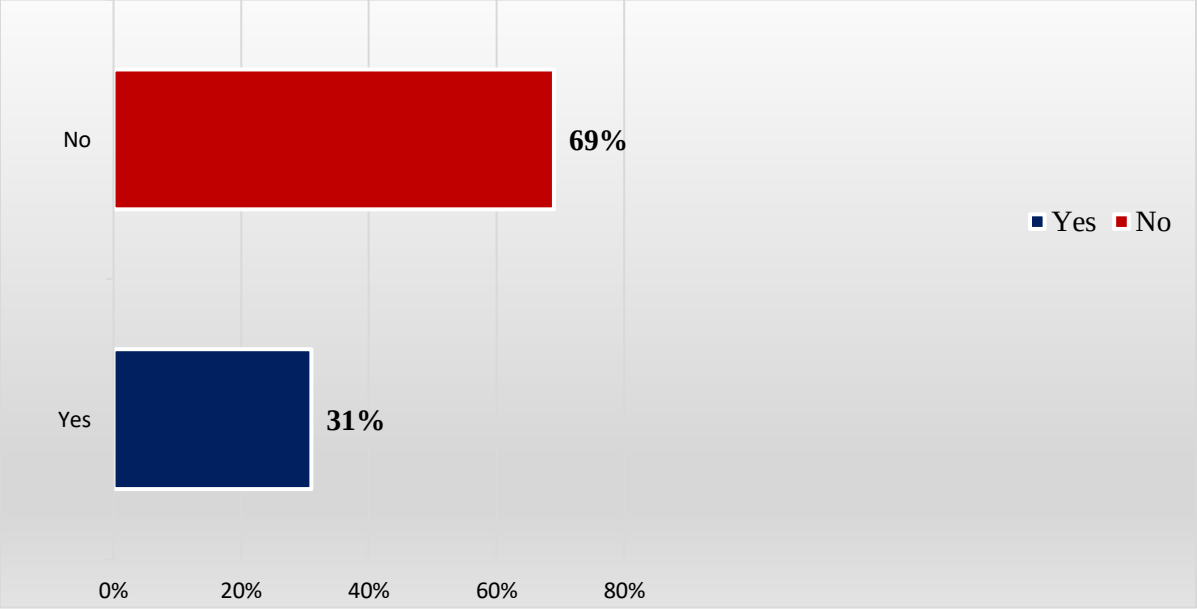


Figure 14: Cost of treatment

The cost of higher for 69% of the people who is getting treatment for cancer and also it is hampering their family life.

What do you think about future of cancer treatment in Bangladesh?

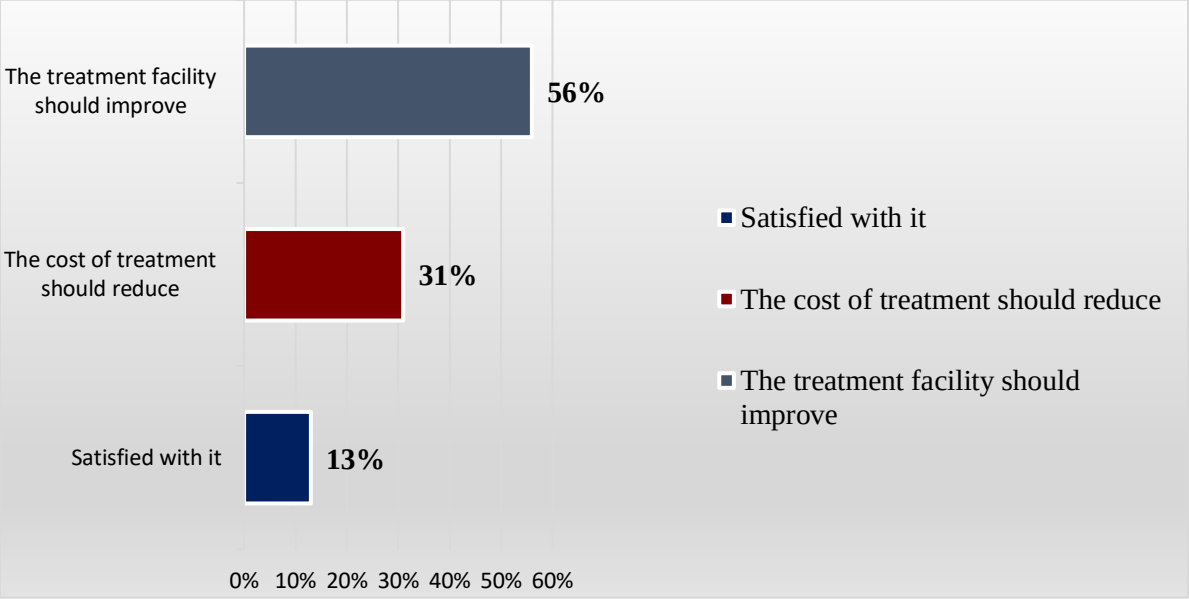


Figure 15: Future of cancer treatment

Only 13% of think that the treatment they are getting good enough for them but other 87% people are not happy with it.

5.2 Discussion

The primary findings from the Joint Group on Epidemiological Investigations of Ovarian Cancer and a network of case-control studies conducted in Italy are included in the current review of ovarian cancer epidemiology. The probability of ovarian cancer is consistently inversely correlated with parity and the usage of oral contraceptives. There are known connections for other menstrual or hormonal variables (such as young age at menarche as well as late menopause), but their influence on the risk of ovarian cancer in the general population is limited. Hormone replacement medication used after menopause, both recently and now, has been linked to ovarian cancers that are serous and endometriosis (but not mucinous or pure cell types). The risk of ovarian cancer is directly correlated with height and BMI; it may also be inversely correlated with physical activity and have potential relationships with certain dietary components, however consistent results have not been found. A family record of ovarian cancer (as well as a few other specific neoplasms, such as colonic and endometrial neoplasms) is strongly associated. Only a small percentage of ovarian cancer incidences in the general population may be attributed to known risk factors.

To understand the actual perception of the local people this survey was conducted from August 5 to November 10, 2023. A total of 200 ovarian cancer patients were interviewed the responder's average age was between 41-70 years 65%. 41-70 years old peoples are most prone to develop Ovarian Cancer. Above 70 years are also very risky in this scenario. The majority of respondents were having loss and also feeling tiredness. According to the respondent's, the majority of people is suffering from this problem for more than 1 year. Majority of people is suffering from this problem is thinking about surgery or going to surgery very soon. Almost half of the people who is getting treatment for cancer unsatisfied with the treatment they are getting for their diseases. The cost of higher for 69% of the people who is getting treatment for cancer and also it is hampering their family life. Only 13% of think that the treatment they are getting good enough for them but other 87% people are not happy with it.

CHAPTER 6

CONCLUSION

6. Conclusion

Ovarian Cancer is growing as a major health concern for Bangladesh. The women with older age suffer more with this diseases. The findings from that survey suggested that it's the women whose age is more than 40 is mostly affected by this diseases. The major reason behind it is that they suffer from urinary tract infection most often if the problem remain untreated it can effect in the major way. Also the people in our country tend to ignore the early symptoms of this diseases and this things become a major problem and develop ovarian cancer at the end. The present treatment for this diseases in our country is developing but the cost is very high for any middle class or lower middle class family. Even the highest treatment standard is not achievable for them. For the future the treatment facility also the cost of the treatment should be reduced so that the patient from different financial should able get the same treatment. The awareness program for this should also increase to educate peoples about this diseases. This thing will make the peoples able to understand the early symptoms of the diseases and get the cure easily. Patient's knowledge about this diseases and who to be cured is also important. If they know about this problems they will get the treatment from the first stage before going into the metastasis phase. The life of patients of this diseases can be saved and the mortality rate will reduce gradually from this diseases.

CHAPTER 7

REFERENCES

Reference

1. ayson, G. C., Kohn, E. C., Kitchener, H. C., & Ledermann, J. A. (2014). Ovarian cancer. *The Lancet*, *384*(9951), 1376-1388.
2. Matulonis, U. A., Sood, A. K., Fallowfield, L., Howitt, B. E., Sehouli, J., & Karlan, B. Y. (2016). Ovarian cancer. *Nature reviews Disease primers*, *2*(1), 1-22.
3. Cho, K. R., & Shih, I. M. (2009). Ovarian cancer. *Annual review of pathology: mechanisms of disease*, *4*, 287-313.
4. Colombo, N., Van Gorp, T., Parma, G., Amant, F., Gatta, G., Sessa, C., & Vergote, I. (2006). Ovarian cancer. *Critical reviews in oncology/hematology*, *60*(2), 159-179.
5. Stewart, C., Ralyea, C., & Lockwood, S. (2019, April). Ovarian cancer: an integrated review. In *Seminars in oncology nursing* (Vol. 35, No. 2, pp. 151-156). WB Saunders.
6. La Vecchia, C. (2017). Ovarian cancer. *European journal of cancer prevention*, *26*(1), 55-62.
7. Permuth-Wey, J., & Sellers, T. A. (2009). Epidemiology of ovarian cancer. *Cancer epidemiology: modifiable factors*, 413-437.
8. Lengyel, E. (2010). Ovarian cancer development and metastasis. *The American journal of pathology*, *177*(3), 1053-1064.
9. Reid, B. M., Permuth, J. B., & Sellers, T. A. (2017). Epidemiology of ovarian cancer: a review. *Cancer biology & medicine*, *14*(1), 9.
10. Islam MR, Rahman MM, Dhar PS, Nowrin FT, Sultana N, Akter M, Rauf A, Khalil AA, Gianoncelli A, Ribaudo G. The Role of Natural and Semi-Synthetic Compounds in Ovarian Cancer: Updates on Mechanisms of Action, Current Trends and Perspectives. Molecules. 2023 Feb 22;28(5):2070. doi: 10.3390/molecules28052070. PMID: 36903316; PMCID: PMC10004182.
11. Subhan A, Attia SA, P Torchilin V. Targeted siRNA nanotherapeutics against breast and ovarian metastatic cancer: a comprehensive review of the literature. Nanomedicine (Lond). 2022 Jan;17(1):41-64. doi: 10.2217/nnm-2021-0207. Epub 2021 Dec 21. PMID: 34930021.
12. Morand S, Devanaboyina M, Staats H, Stanbery L, Nemunaitis J. Ovarian Cancer Immunotherapy and Personalized Medicine. Int J Mol Sci. 2021 Jun 18;22(12):6532. doi: 10.3390/ijms22126532. PMID: 34207103; PMCID: PMC8234871.

13. Stewart C, Ralyea C, Lockwood S. Ovarian Cancer: An Integrated Review. Semin Oncol Nurs. 2019 Apr;35(2):151-156. doi: 10.1016/j.soncn.2019.02.001. Epub 2019 Mar 11. PMID: 30867104.
14. Webb PM, Jordan SJ. Epidemiology of epithelial ovarian cancer. Best Pract Res Clin Obstet Gynaecol. 2017 May;41:3-14. doi: 10.1016/j.bpobgyn.2016.08.006. Epub 2016 Oct 3. PMID: 27743768.
15. Cho KR, Shih IeM. Ovarian cancer. Annu Rev Pathol. 2009;4:287-313. doi: 10.1146/annurev.pathol.4.110807.092246. PMID: 18842102; PMCID: PMC2679364.
16. Eisenhauer EA. Real-world evidence in the treatment of ovarian cancer. Ann Oncol. 2017 Nov 1;28(suppl_8):viii61-viii65. doi: 10.1093/annonc/mdx443. PMID: 29232466.
17. Matulonis UA. Ovarian Cancer. Hematol Oncol Clin North Am. 2018 Dec;32(6):xiii-xiv. doi: 10.1016/j.hoc.2018.09.006. Epub 2018 Sep 25. PMID: 30390771.
18. O'Shea AS. Clinical Staging of Ovarian Cancer. Methods Mol Biol. 2022;2424:3-10. doi: 10.1007/978-1-0716-1956-8_1. PMID: 34918284.
19. Rooth C. Ovarian cancer: risk factors, treatment and management. Br J Nurs. 2013 Sep 12-25;22(17):S23-30. doi: 10.12968/bjon.2013.22.Sup17.S23. PMID: 24067270.
20. O'Malley DM. New Therapies for Ovarian Cancer. J Natl Compr Canc Netw. 2019 May 1;17(5.5):619-621. doi: 10.6004/jnccn.2019.5018. PMID: 31117037.
21. Dong X, Men X, Zhang W, Lei P. Advances in tumor markers of ovarian cancer for early diagnosis. Indian J Cancer. 2014 Mar;51 Suppl 3:e72-6. doi: 10.4103/0019-509X.154049. PMID: 25818738.
22. Sipos A, Ujlaki G, Mikó E, Maka E, Szabó J, Uray K, Krasznai Z, Bai P. The role of the microbiome in ovarian cancer: mechanistic insights into oncobiosis and to bacterial metabolite signaling. Mol Med. 2021 Apr 1;27(1):33. doi: 10.1186/s10020-021-00295-2. PMID: 33794773; PMCID: PMC8017782.
23. Wang JY, Lu AQ, Chen LJ. LncRNAs in ovarian cancer. Clin Chim Acta. 2019 Mar;490:17-27. doi: 10.1016/j.cca.2018.12.013. Epub 2018 Dec 13. PMID: 30553863.
24. Ottevanger PB. Ovarian cancer stem cells more questions than answers. Semin Cancer Biol. 2017 Jun;44:67-71. doi: 10.1016/j.semcancer.2017.04.009. Epub 2017 Apr 24. PMID: 28450177.

25. Ottevanger PB. Ovarian cancer stem cells more questions than answers. Semin Cancer Biol. 2017 Jun;44:67-71. doi: 10.1016/j.semcancer.2017.04.009. Epub 2017 Apr 24. PMID: 28450177.
26. Barua A, Bahr JM. Ovarian Cancer: Applications of Chickens to Humans. Annu Rev Anim Biosci. 2022 Feb 15;10:241-257. doi: 10.1146/annurev-animal-021419-084001. PMID: 35167319.
27. Martin VR. Ovarian cancer. Semin Oncol Nurs. 2002 Aug;18(3):174-83. doi: 10.1053/sonu.2002.34078. PMID: 12184040.
28. Frey MK, Finch A, Kulkarni A, Akbari MR, Chapman-Davis E. Genetic Testing for All: Overcoming Disparities in Ovarian Cancer Genetic Testing. Am Soc Clin Oncol Educ Book. 2022 Apr;42:1-12. doi: 10.1200/EDBK_350292. PMID: 35452249.
29. Konstantinopoulos PA, Matulonis UA. Clinical and translational advances in ovarian cancer therapy. Nat Cancer. 2023 Sep;4(9):1239-1257. doi: 10.1038/s43018-023-00617-9. Epub 2023 Aug 31. PMID: 37653142.
30. Ozols RF, Young RC. Ovarian cancer. Curr Probl Cancer. 1987 Mar-Apr;11(2):57-122. doi: 10.1016/s0147-0272(87)80004-1. PMID: 3556023.
31. Vergote I, Harter P, Chiva L. Hyperthermic intraperitoneal chemotherapy does not improve survival in advanced ovarian cancer. Cancer. 2019 Dec 15;125 Suppl 24:4594-4597. doi: 10.1002/cncr.32496. PMID: 31967685.
32. van Nagell JR Jr, Copeland LJ. Ovarian cancer. Foreword. Clin Obstet Gynecol. 2012 Mar;55(1):1-2. doi: 10.1097/GRF.0b013e31824c686b. PMID: 22343224.
33. Mahoney DE, Pierce JD. Ovarian Cancer Symptom Clusters: Use of the NIH Symptom Science Model for Precision in Symptom Recognition and Management. Clin J Oncol Nurs. 2022 Sep 15;26(5):533-542. doi: 10.1188/22.CJON.533-542. PMID: 36108208; PMCID: PMC9951395.
34. Ovarian Cancer. Am Fam Physician. 2016 Jun 1;93(11):Online. PMID: 27281844.
35. Richardson GS. Ovarian cancer. JAMA. 1993 Mar 3;269(9):1163. PMID: 8433473.
36. Permuth-Wey, J., & Sellers, T. A. (2009). Epidemiology of ovarian cancer. *Cancer epidemiology: modifiable factors*, 413-437.
37. Lengyel, E. (2010). Ovarian cancer development and metastasis. *The American journal of pathology*, *177*(3), 1053-1064.

38. Reid, B. M., Permuth, J. B., & Sellers, T. A. (2017). Epidemiology of ovarian cancer: a review. *Cancer biology & medicine*, *14*(1), 9.
39. Berek, J. S., & Bast, R. C. J. (1985). Ovarian cancer.
40. Roett, M. A., & Evans, P. (2009). Ovarian cancer: an overview. *American family physician*, *80*(6), 609-616.
41. Auersperg, N., Edelson, M. I., Mok, S. C., Johnson, S. W., & Hamilton, T. C. (1998, June). The biology of ovarian cancer. In *Seminars in oncology* (Vol. 25, No. 3, pp. 281-304).
42. Auersperg, N., Edelson, M. I., Mok, S. C., Johnson, S. W., & Hamilton, T. C. (1998, June). The biology of ovarian cancer. In *Seminars in oncology* (Vol. 25, No. 3, pp. 281-304).
43. Clarke-Pearson, D. L. (2009). Screening for ovarian cancer. *New England Journal of Medicine*, *361*(2), 170-177.
44. Carlson, K. J., Skates, S. J., & Singer, D. E. (1994). Screening for ovarian cancer. *Annals of internal medicine*, *121*(2), 124-132.
45. Doubeni, C. A., Doubeni, A. R., & Myers, A. E. (2016). Diagnosis and management of ovarian cancer. *American family physician*, *93*(11), 937-944.
46. Jelovac, D., & Armstrong, D. K. (2011). Recent progress in the diagnosis and treatment of ovarian cancer. *CA: a cancer journal for clinicians*, *61*(3), 183-203.
47. Lheureux, S., Gourley, C., Vergote, I., & Oza, A. M. (2019). Epithelial ovarian cancer. *The Lancet*, *393*(10177), 1240-1253.
48. Aletti, G. D., Gallenberg, M. M., Cliby, W. A., Jatoi, A., & Hartmann, L. C. (2007, June). Current management strategies for ovarian cancer. In *Mayo Clinic Proceedings* (Vol. 82, No. 6, pp. 751-770). Elsevier.
49. Chobanian, N., & Dietrich III, C. S. (2008). Ovarian cancer. *Surgical Clinics of North America*, *88*(2), 285-299.
50. Sundar, S., Neal, R. D., & Kehoe, S. (2015). Diagnosis of ovarian cancer. *Bmj*, *351*.
51. Burges, A., & Schmalfeldt, B. (2011). Ovarian cancer: diagnosis and treatment. *Deutsches Ärzteblatt International*, *108*(38), 635.
52. Torre, L. A., Trabert, B., DeSantis, C. E., Miller, K. D., Samimi, G., Runowicz, C. D., ... & Siegel, R. L. (2018). Ovarian cancer statistics, 2018. *CA: a cancer journal for clinicians*, *68*(4), 284-296.

53. Cortez, A. J., Tudrej, P., Kujawa, K. A., & Lisowska, K. M. (2018). Advances in ovarian cancer therapy. *Cancer chemotherapy and pharmacology*, *81*, 17-38.
54. La Vecchia, C. (2001). Epidemiology of ovarian cancer: a summary review. *European Journal of Cancer Prevention*, *10*(2), 125-129.
55. Gaona-Luviano, P., Medina-Gaona, L. A., & Magaña-Pérez, K. (2020). Epidemiology of ovarian cancer. *Chin Clin Oncol*, *9*(4), 47.
56. Kossaï, M., Leary, A., Scoazec, J. Y., & Genestie, C. (2018). Ovarian cancer: a heterogeneous disease. *Pathobiology*, *85*(1-2), 41-49.
57. Momenimovahed, Z., Tiznobaik, A., Taheri, S., & Salehiniya, H. (2019). Ovarian cancer in the world: epidemiology and risk factors. *International journal of women's health*, 287-299.
58. Prat, J., Ribé, A., & Gallardo, A. (2005). Hereditary ovarian cancer. *Human pathology*, *36*(8), 861-870.
59. Deb, B., Uddin, A., & Chakraborty, S. (2018). miRNAs and ovarian cancer: An overview. *Journal of cellular physiology*, *233*(5), 3846-3854.
60. Young RC. Ovarian cancer. CA Cancer J Clin. 1995 Mar-Apr;45(2):69-70. doi: 10.3322/canjclin.45.2.69. PMID: 7889391.
61. Wenham RM. Ovarian cancer: a bright future. Cancer Control. 2011 Jan;18(1):4-5. doi: 10.1177/107327481101800101. PMID: 21273974.
62. Bukłaho PA, Kiśluk J, Wasilewska N, Nikliński J. Molecular features as promising biomarkers in ovarian cancer. Adv Clin Exp Med. 2023 Sep;32(9):1029-1040. doi: 10.17219/acem/159799. PMID: 36920264.
63. Mantia-Smaldone GM, Corr B, Chu CS. Immunotherapy in ovarian cancer. Hum Vaccin Immunother. 2012 Sep;8(9):1179-91. doi: 10.4161/hv.20738. Epub 2012 Aug 21. PMID: 22906947; PMCID: PMC3579897.
64. Cragun JM. Screening for ovarian cancer. Cancer Control. 2011 Jan;18(1):16-21. doi: 10.1177/107327481101800103. PMID: 21273976.
65. Karam AK, Karlan BY. Ovarian cancer: the duplicity of CA125 measurement. Nat Rev Clin Oncol. 2010 Jun;7(6):335-9. doi: 10.1038/nrclinonc.2010.44. Epub 2010 Apr 6. PMID: 20368726.

66. Hennessy BT, Coleman RL, Markman M. Ovarian cancer. Lancet. 2009 Oct 17;374(9698):1371-82. doi: 10.1016/S0140-6736(09)61338-6. Epub 2009 Sep 28. PMID: 19793610.
67. Einhorn N. Ovarian cancer. Acta Oncol. 1996;35 Suppl 7:86-92. doi: 10.3109/02841869609101668. PMID: 9154100.
68. Tew WP, Lichtman SM. Ovarian cancer in older women. Semin Oncol. 2008 Dec;35(6):582-9. doi: 10.1053/j.seminoncol.2008.08.007. PMID: 19027462.
69. Malander S, Hjerpe E, Carlson J, Borg Å. Ovarialcancer är på många sätt en heterogen sjukdom [Ovarian cancer is in many ways a heterogeneous disease]. Lakartidningen. 2015 Dec 8;112:DIUR. Swedish. PMID: 26646956.
70. Annunziata CM, Azad N, Dhamoon AS, Whiteley G, Kohn EC. Ovarian cancer in the proteomics era. Int J Gynecol Cancer. 2008 Mar-Apr;18 Suppl 1:1-6. doi: 10.1111/j.1525-1438.2007.01096.x. PMID: 18336391.
71. Barber HR, Graber EA, KwonTH. Ovarian cancer. CA Cancer J Clin. 1974 Nov-Dec;24(6):339-50. doi: 10.3322/canjclin.24.6.339. PMID: 4216394.
72. Banerjee, S., Tian, T., Wei, Z., Shih, N., Feldman, M. D., Alwine, J. C., ... & Robertson, E. S. (2017). The ovarian cancer oncobiome. *Oncotarget*, *8*(22), 36225.
73. Tortolero-Luna, G., & Mitchell, M. F. (1995). The epidemiology of ovarian cancer. *Journal of Cellular Biochemistry*, *59*(S23), 200-207.
74. Hanna, L., & Adams, M. (2006). Prevention of ovarian cancer. *Best Practice & Research Clinical Obstetrics & Gynaecology*, *20*(2), 339-362.
75. Hoskins, W. J. (1995). Prospective on ovarian cancer: why prevent?. *Journal of Cellular Biochemistry*, *59*(S23), 189-199.
76. Marcus, C. S., Maxwell, G. L., Darcy, K. M., Hamilton, C. A., & McGuire, W. P. (2014). Current approaches and challenges in managing and monitoring treatment response in ovarian cancer. *Journal of Cancer*, *5*(1), 25.
77. Kurnit, K. C., Fleming, G. F., & Lengyel, E. (2021). Updates and new options in advanced epithelial ovarian cancer treatment. *Obstetrics and gynecology*, *137*(1), 108.
78. Earle, C. C., Schrag, D., Neville, B. A., Yabroff, K. R., Topor, M., Fahey, A., ... & Warren, J. L. (2006). Effect of surgeon specialty on processes of care and outcomes for ovarian cancer patients. *Journal of the National Cancer Institute*, *98*(3), 172-180.