Chapter 1

INTRODUCTION
CHAPTER-I
INTRODUCTION

“If we have any chance at prevention,
then we women should do something about it”

Cervical cancer is the top cancer observed among women in most East African and South Asian countries both in terms of incidence and mortality. In 2008, approximately 530,000 women were diagnosed with invasive cervical cancer worldwide and 275,000 women died from it. Indeed, developing countries as a whole experience a disproportionate share of the disease burden, accounting for 86% of all cervical cancer cases and 88% of all cervical cancer deaths worldwide (Jemal, 2011). Developing countries have over 80 per cent of the world’s burden of cancer of the cervix with India having one fourth of the world’s burden of the disease. Cancer of the cervix has declined significantly in industrialized countries in the last several decades mainly due to their implementation of effective population based prevention programmes (WHO, 2002). While cervical cancer rates have declined markedly in industrialized countries over the past several decades, the rates have declined at a much slower pace in the developing world and, for many developing countries, the rates have actually been increasing.

The data from the World Health Organization (WHO) show marked disparities in cervical cancer incidence and mortality rates across countries (Ferlay et al, 2008). Cervical cancer, the third most common cancer among women in the world, was responsible for 275,000 deaths in 2008, 88 per cent of which occurred in developing countries and 159,800 in Asia. Cervical cancer is generally defined as a disease of disparity. This is due to marked differences in the incidence and mortality
of cervical cancer between the developed and developing world. According to the Crisis Card, the mortality rate is the highest in Africa. Australia has the lowest cervical cancer mortality rate, which is due to the successful rollout of a comprehensive package of HPV vaccines, treatment and prevention.

Cervical cancer is the 12th most common cancer among women females in the UK (2010), accounting for around 2% of all new cases of cancer in females. In 2010, there were 2,851 new cases of cervical cancer in the UK. The crude incidence rate shows that there are around 9 new cervical cancer cases for every 100,000 females in the UK. According to the International Agency for Research on Cancer, annually worldwide registered 530,000 new cases of cervical cancer are registered with 275,000 mortalities. It is also the most common cause of cancer death (266,000 deaths in 2012) in women worldwide.

Lower cancer survival and higher mortality rates partly result from higher rates of late-stage cancer diagnosis among women in developing countries, which are largely due to the lack of effective cervical cancer screening programs. About 81% of cervical cancer patients in Singapore are diagnosed at an early, localized stage, compared with only 7% in Chennai, India, 33% in Costa Rica, 35% in Manila, Philippines, and 53% in Cuba (Gakidou, 2008). The high rate of early-stage diagnosis in Singapore is higher than the rate for many industrialized countries, including the United States, where only 52% of invasive cervical cancers in 2008 were diagnosed at localized stage (Howlader et al, 2008). Detection of cancer at an early stage may be considered a marker for access to health care and preventive health services, including cervical cancer screening. Cancer incidence is generally expressed as Age Adjusted or Age Standardized Incidence Rates (AAR) per 100,000 persons according to world standard population.
1.1 Cervical Cancer in India

India has the highest number of deaths from cervical cancer than any other country. According to a new report, deaths from this preventable disease will rise unless attitudes of women change. One in every five women in the world suffering from cervical cancer belongs to India which has the largest burden of cervical cancer patients in the world. The disease consumes resources at a staggering rate in the way of medical, non-medical spending and lost productivity. Although cervical cancer is the most frequent cancer diagnosed in Indian women, age-adjusted incidence rates vary from 8.8 per 100,000 women to 10.1 per 100,000 women.

In India, each year cervical cancer accounts for 26.7 percent of worldwide incidence and 72,825 Indian women die due to cervical cancer. It is a major cause of morbidity and mortality more than 1, 32,000 women are diagnosed with cervical cancer every year, In fact 200 women are dying every 24 hours in India due to cervical cancer. In Uttar Pradesh a total of 17367 cases were reported in 2009 and they increased to 18692 in 2012. After Uttar Pradesh, the number of cases of cervical cancer in 2012 which has shown an increasing trend are Maharashtra (9892), Bihar (9824), West Bengal (8396), Andhra Pradesh (7907), Tamil Nadu (7077) and others. In India, the onus of preventing cervical cancer is on the women themselves. Therefore, it is the woman’s knowledge level, motivation for screening and other psychosocial factors that determine her health seeking behaviour.

India has a disproportionately high burden of cervical cancer (Shanta et al, 2000). Although its age standardized death rate of 9.5 deaths per 100,000 population is representative of global rates, it accounts for nearly one-third of global cervical cancer deaths (WHO 2009b, GLOBOCAN 2008, IARC 2009). Cervical cancer is the
third largest cause of cancer mortality in India after cancers of the mouth & oropharynx, and oesophagus, accounting for nearly 10% of all cancer related deaths in the country (WHO, 2009b). Among women, it is the leading cause of cancer mortality, accounting for 26% of all cancer deaths (GLOBOCAN 2008). According to IARC estimates (2010), mortality from cervical cancer is expected to witness a 79% increase from 74,118 deaths in 2002 to 132,745 deaths by 2025 (National Cancer Registry Programme 2009, WHO 2004).

1.1.1 Economic Burden of Cervical Cancer

Cervical cancer causes loss of productive life both due to early death as well as prolonged disability (WHO, 2009b). In India, the Years of Life Lost (YLL) due to cervical cancer were 936 in 2000, being among the highest in the world, greater than the YYLs caused by any other cancer in India, and constituting almost 4% of total YYLs due to all causes in India (Yang et al, 2004). Among women aged 25-64 years, who tend, in India, to be the sole caretakers of the house & family, and in some cases significant contributors to the family income, this mortality burden poses a heavy economic burden on families (Arrossi et al, 2007), as well the country (National Commission on Macroeconomics of Health, 2005). Additionally, the high medical costs that are incurred by families due to cervical cancer (especially since most cases in developing countries are diagnosed at advanced stages when treatment is costly but prognosis poor), further impoverish individuals and communities (Bishop et al, 1996).

The cost of secondary care of invasive cervical cancer is another source of economic burden. According to the National Commission on Macroeconomics of Health report (2005), the per unit cost of providing secondary care for cervical cancer at the level of district hospitals is 10,016.04 INR, higher than that of all other chronic
conditions with the exception of cardiovascular diseases. Due to the high number of cervical cancer cases in the population, India has the highest total cost of secondary care (100,000 INR per 100,000 populations) relative to all other cancers. Recognizing the high costs incurred in secondary care of cervical cancer it is suggested that, prevention through screening and vaccination may be a more cost-effective option for India. Cancer of the cervix is a common cancer that afflicts Indian woman - physically, psychologically, socially and financially. This disease affects not just the woman but also her family and the society. It is estimated that yearly 1,34,420 Indian women are newly diagnosed with cancer of the cervix and each year the disease kills an estimated 72,825 Indian women.

1.2 Cancer

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly fashion. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell. Cells become cancer cells because of damage to DNA. DNA will be in every cell and directs all its actions. Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.
1.3 Cervical Cancer

Cervical cancer is a disease in which the cells of the cervix become abnormal and start to grow uncontrollably, forming tumors.

The cervix is the lower part of the uterus (womb). It is sometimes called uterine cervix. The fetus grows in the body of the uterus (upper part). The cervix connects the body of the uterus to the vagina (Birth canal). The part of the cervix close to the body of the uterus is called the endo-cervix. The two main types of cells covering the cervix or squamous cells (on the exo-cervix) and glandular cells (on the endocervix). These 2 cell types meet at a place called the transformation zone. Most cervical cancers start in the transformation zone. Most cervical cancers begin in the cells lining the cervix. These cells do not suddenly change into cancer. Instead, the normal cells of the cervix first gradually develop pre-cancerous changes that turn into cancer.

There are two main types of cervical cancers: squamous cell carcinoma and adenocarcinoma. Cancer that develops in the ectocervix is called squamous cell carcinoma, and around 80-90% of cervical cancer cases (more than 90% in India) are of this type [WHO/ICO Information Centre on HPV and Cervical Cancer]. Cancer that develops in the endocervix is called adenocarcinoma. In addition, a small percentage of cervical cancer cases are mixed versions of the above two, and are called adenosquamous carcinomas or mixed carcinomas. There are also some very rare types of cervical cancer, such as small cell carcinoma, neuroendocrine carcinoma etc. (American Cancer Society). The rest of this discussion will focus on the first two types, as they constitute the greatest burden, globally as well as in India.
1.4 Risk Factors for Cervical Cancer

A risk factor is anything that changes the chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for many cancers. But having a risk factor, or even several, does not mean that cancer will be affected. Several risk factors increase the chance of developing cervical cancer. Women without any of these risk factors rarely develop cervical cancer. Although these risk factors increase the odds of developing cervical cancer, many women with these risks do not develop this disease. When a woman develops cervical cancer or pre-cancerous changes, it may not be possible to say with certainty that a particular risk factor was the cause. In thinking about risk factors, it helps to focus on those that can change or avoid (like smoking or human papilloma virus infection), rather than those that cannot (such as your age and family history). However, it is still important to know about risk factors that cannot be changed, because it's even more important for women who have these factors to get regular Pap tests to detect cervical cancer early.

1.4.1 Human papilloma virus

The main risk factor for the development of cervical cancer is human papilloma virus (HPV) infection, DNA of which has been found in almost all cases of invasive cervical cancer (Bosch and de Sanjosé, 2003). HPV is a sexually transmitted infection, making cervical cancer a chronic disease with an infectious aetiology (Alliance for Cervical Cancer Prevention, Cancer Research UK). At least 50% of sexually active men and women get HPV at some point in their lives [Centers for Disease Control and Prevention (c)]. Most women with HPV infection will not
develop cancer, and the infection usually resolves spontaneously; however, around 3-10% of women with HPV develops persistent infections, and are at high risk of developing cervical cancer (Monsonego et al, 2004).

HPV is a group of more than 150 related viruses, some of which cause a type of growth called a papilloma, which are more commonly known as warts. HPV can infect cells on the surface of the skin, and those lining the genitals, anus, mouth and throat, but not the blood or internal organs such as the heart or lungs. HPV can be passed from one person to another during skin-to-skin contact. One way HPV is spread is through sex, including vaginal and anal intercourse and even oral sex. Different types of HPVs cause warts on different parts of the body. Some cause common warts on the hands and feet; others tend to cause warts on the lips or tongue. Certain types of HPV may cause warts on or around the female and male genital organs and in the anal area. These warts may barely be visible or they may be several inches across. These are known as genital warts or condyloma acuminatum. Most cases of genital warts are caused by HPV 6 and HPV 11. They are called low-risk types of HPV because they are seldom linked to cancer. Other types of HPV are called high-risk types because they are strongly linked to cancers, including cancer of the cervix, vulva, and vagina in women, penile cancer in men, and cancers of the anus, mouth, and throat in both men and women.

Although there are several strains of HPV infection, (most of which have been found to increase the risk of developing cervical cancer) two strains: HPV 16 and 18, account for more than 70% of all cervical cancer cases; five other strains: HPV 31, 33, 35, 45, 52 and 58 account for an additional 20%. The level of sexual activity of a person will affect the risk of acquiring HPV infection. Early age of first intercourse, multiple sexual partners, unprotected sex and sex with uncircumcised
men, have been found to increase the risk of contracting HPV infection (Franceschi et al, 2003; World Health Organisation, 2006; Biswas et al, 1997). For example, having more than 3 sexual partners during a woman’s lifetime will increase the risk of cervical cancer by 94% compared to women with one lifetime partner. Among men, high lifetime number of sexual partners [multivariate OR for 2-9 partners relative to none 2.11 (1.17-3.78)] and recent number of sexual partners [multivariate OR for 2 partners in 3 months relative to none 2.09 (1.25-3.49)] have been found to increase the risk of contracting HPV infection, while not having had sex in the past 3 months [multivariate OR 0.42 (0.22-0.81)] and circumcision [multivariate OR 0.70 (0.52-0.94)] have been found to have a protective effect (Giuliano et al, 2009).

There are additional factors that increase the risk of developing cervical cancer after contracting HPV infection. These include smoking, oral contraceptive use, high parity, and infection with other sexually transmitted diseases such as HIV, Herpes, Chlamydia, gonorrhoea, and syphilis (de González et al, 2004; Plummer et al, 2003; Moreno et al, 2002; International Collaboration of Epidemiological Studies of Cervical Cancer, 2007; Smith et al, 2003; Muñoz et al, 2002) González et al, 2004). For example, high parity (3 births or more) increases the risk of cervical cancer by 51% compared to women who had not given birth.

1.4.2 Other factors

The high-risk types include HPV 16, HPV 18, HPV 31, HPV 33, and HPV 45, as well as some others. There might be no visible signs of infection with a high-risk HPV until pre-cancerous changes or cancer develops.
1.4.3 Smoking

When someone smokes, they and those around them are exposed to many cancer-causing chemicals that affect organs other than the lungs. These harmful substances are absorbed through the lungs and carried in the bloodstream throughout the body. Women who smoke are about twice as likely as non-smokers to get cervical cancer. Tobacco by-products have been found in the cervical mucus of women who smoke. Researchers believe that these substances damage the DNA of cervix cells and may contribute to the development of cervical cancer. Smoking also makes the immune system less effective in fighting HPV infections.

1.4.4 Immune suppression

Human immunodeficiency virus (HIV), the virus that causes AIDS, damages the immune system and puts women at higher risk for HPV infections. This might explain why women with AIDS have an increased risk for cervical cancer. The immune system is important in destroying cancer cells and slowing their growth and spread. In women with HIV, a cervical pre-cancer might develop into an invasive cancer faster than it normally would. Another group of women at risk of cervical cancer are women receiving drugs to suppress their immune response, such as those being treated for an autoimmune disease (in which the immune system sees the body's own tissues as foreign and attacks them, or those who have had an organ transplant.

1.4.5 Chlamydia infection

Chlamydia is a relatively common kind of bacteria that can infect the reproductive system. It is spread by sexual contact. Chlamydia infection can cause pelvic inflammation, leading to infertility. Some studies have seen a higher risk of
cervical cancer in women whose blood test results show evidence of past or current chlamydia infection (compared with women who have normal test results). Women who are infected with chlamydia often have no symptoms. In fact, they may not know that they are infected at all unless they are tested for Chlamydia during a pelvic exam.

1.4.6 Diet

Women whose diets don’t include enough fruits and vegetables may be at increased risk for cervical cancer. Overweight women are more likely to develop adenocarcinoma of the cervix.

1.4.7 Oral contraceptives (birth control pills)

There is evidence that taking oral contraceptives (OCs) for a long time increases the risk of cancer of the cervix. Research suggests that the risk of cervical cancer goes up the longer a woman takes OCs, but the risk goes back down again after the OCs are stopped. In one study, the risk of cervical cancer was doubled in women who took birth control pills longer than 5 years, but the risk returned to normal 10 years after they were stopped. The American Cancer Society believes that a woman and her doctor should discuss whether the benefits of using OCs outweigh the potential risks. A woman with multiple sexual partners should use condoms to lower her risk of sexually transmitted illnesses no matter what other form of contraception she uses.

1.4.8 Intrauterine device use

A recent study found that women who had ever used an intrauterine device (IUD) had a lower risk of cervical cancer. The effect on risk was seen even in women who had an IUD for less than a year, and the protective effect remained after the IUDs
were removed. Using an IUD might also lower the risk of endometrial (uterine) cancer. However, IUDs do have some risks. Also, a woman with multiple sexual partners should use condoms to lower her risk of sexually transmitted illnesses no matter what other form of contraception she uses.

1.4.9 Multiple full-term pregnancies

Women who have had 3 or more full-term pregnancies have an increased risk of developing cervical cancer. This may be due to the fact that these women had to have had unprotected intercourse to get pregnant and thereby they may have had more exposure to HPV. Also, studies have shown that hormonal changes during pregnancy make women more susceptible to HPV infection or cancer growth. Another thought is that pregnant women might have weaker immune systems, allowing for HPV infection and cancer growth. Women who were younger than 17 years when they had their first full-term pregnancy are almost 2 times more likely to get cervical cancer later in life than women who waited to get pregnant until they were 25 years or older.

1.4.10 Poverty

Poverty is also a risk factor for cervical cancer. Many low-income women do not have ready access to adequate health care services, including Pap tests. This means they may not get screened or treated for cervical pre-cancers.

1.4.11 Family history of cervical cancer

Some researchers suspect that some instances of this familial tendency to develop the disease are 2 to 3 times higher than those that are caused by an inherited condition that makes some women less able to fight off HPV infection than others. In
other instances, women from the same family as a patient already diagnosed could be more likely to have one or more of the other non-genetic risk factors.

Other risk factors like a woman's sexual habits and patterns can increase her risk of developing cervical cancer. Risky sexual practices include:

- Having sex at an early age
- Having multiple sexual partners
- Having a partner or many partners who are active in high-risk sexual activities

1.5 Symptoms of Cervical Cancer

Most women with dysplasia or pre-invasive cancer have no symptoms. Screening tests, therefore, are very important. When cancer becomes invasive, unusual bleeding can occur. Bleeding may stop and start again between regular periods or there may be bleeding after menopause. Unexpected bleeding can also occur after intercourse or a pelvic exam. Periods sometimes last longer or are heavier than usual. Increased vaginal discharge may be noticeable as well. Pelvic pain or pain during sexual intercourse can occur. These symptoms are not exclusive to cervical cancer. Sexually transmitted diseases, for instance, can cause similar symptoms.

Most of the time, early cervical cancer has no symptoms. Symptoms that may occur include:

- Abnormal vaginal bleeding between periods, after intercourse, or after menopause
- Vaginal discharge that does not stop, and may be pale, watery, pink, brown, bloody, or foul-smelling
- Periods that become heavier and last longer than usual
Cervical cancer may spread to the bladder, intestines, lungs, and liver. Often there are no problems until the cancer is advanced and has spread. Symptoms of advanced cervical cancer may include:

- Back pain
- Bone pain or fractures
- Fatigue
- Leaking of urine or feces from the vagina
- Leg pain
- Loss of appetite
- Pelvic pain
- Single swollen leg
- Weight loss

1.6 Diagnosis and Screening

The changes that lead to cervical cancer develop slowly. Screening tests performed during regular gynecologic examinations can detect early changes.

1.6.1 Pap smear

Use of the Pap smear has significantly reduced the death rate from cervical cancer. Many women who have a Pap smear fail to follow-up for retesting and treatment. Most cases of cervical cancer occur in women who have not had regular Pap tests.

The procedure

The most accurate test results are obtained 12 - 14 days after menstruation begins. Women should not douche or have intercourse within 48 hours of the test.
Douches and spermicidal creams may clean out abnormal cells and interfere with the results of a Pap smear. (In general, douching is not recommended at all.) A Pap smear is usually painless, although some women may have some discomfort.

- The test is done in a doctor's office. The woman removes her clothes from the waist down and puts on a medical gown. She lies on her back on the examination table, bends her knees, and puts her feet in supports (called stirrups) at the end of the table.
- The doctor inserts a plastic or metal device (called a speculum) into her vagina to widen it.
- Using a spatula, brush, or both, the doctor gently scrapes the surface of the cervix, and sometimes the upper vagina, to gather living cells. The doctor will also obtain cells from inside the cervical canal. The scraping is completely painless.
- The cells are preserved, stained for microscopic viewing, and then analyzed under a microscope by a specialist known as a cytopathologist.

1.6.2 Reliability and Accuracy

The Pap smear is not a perfectly reliable measure of a woman's risk for cervical cancer. In general, about 10% of Pap smears have abnormal results, but only about 0.1% of the women who have these results actually have cancer. In most cases, abnormal cells are low grade and not likely to progress to cancer or are due to benign conditions, including natural cell changes after menopause.

- No test is 100% accurate, and it is possible for the Pap smear to miss the presence of cancer. However, if abnormal cells are missed on one test they are likely to be spotted during the next one without a significant danger.
• New tests and methods have been developed to improve the accuracy of the Pap smear in detecting cancer cells. For example, there are several computerized Pap test systems that are used to rescreen the original smear. These systems are either used to detect abnormal samples that may have been missed by manual review methods or are used in place of a human cytotechnologist. There is not yet enough evidence to know whether or not computerized methods are superior to conventional Pap testing.

• Newer, thin-layer liquid based tests (ThinPrep, SurePath) use the original cervical sample, which is rinsed in a special solution to thin the mucus (rather than dried). The fluid is examined for evidence of abnormal cells as well as HPV and other early abnormalities. Some, but not all, studies have found liquid-based Pap tests to be more accurate than the standard Pap smear.

1.6.3 Current Pap Smear Screening Recommendations

General guidelines for cervical cancer screening recommend:

1.6.3.1 Initial Screening

Women should begin to undergo Pap tests at age 21 regardless of whether or not they have been sexually active.

1.6.3.2 Women Up to Age 30

Women between the ages 21 - 29 should be screened for cervical cancer once every 2 years with either a conventional or liquid-based Pap test.

1.6.3.3 Women Age 30 and Over

Women aged 30 and older should be screened for cervical cancer once every 2 years with either a conventional or liquid-based Pap test. Women in this age group who have received three consecutive negative (normal) annual Pap tests may be
screened once every three years with either of these tests. Women who have certain risk factors (HIV-positive, weakened immune system, DES exposure, or prior cervical abnormalities) may need to be screened every year.

1.6.3.4 Elderly Women

Most women can stop cervical cancer screening around age 65 – 70, as long as they have had three negative (normal) Pap tests within the last 10 years.

1.6.3.5 After a Hysterectomy

Women who have had a total hysterectomy (removal of uterus and cervix) for non-cancer reasons may choose to discontinue Pap testing. Women who have had a hysterectomy that preserves the cervix (called a supracervical hysterectomy) should continue with Pap screening.

1.6.4 Colposcopy and Biopsy

The Pap smear shows only the presence of abnormal cells. It is useful simply as a screening test that identifies women who may have preinvasive or early cancerous changes. For a definitive diagnosis, the next step is usually colposcopy, during which the cervix is visualized under low power magnification. The surgeon takes samples of suspicious cells for biopsies. A biopsy will determine the stage of the precancerous growth or whether invasive cancer is present.

1.7 Stages of Cervical cancer

Carcinoma in Situ (Stage 0)

In carcinoma in situ (stage 0), abnormal cells are found in the innermost lining of the cervix. These abnormal cells may become cancerous and spread into nearby normal tissue.
1.7.1 Stage I

In stage I, cancer is found in the cervix only. Stage I is divided into stages IA and IB, based on the amount of cancer that is found.

Stage IA

Stage IA1 and IA2 cervical cancer. A very small amount of cancer that can only be seen with a microscope is found in the tissues of the cervix. In stage IA1, the cancer is not more than 3 millimeters deep and not more than 7 millimeters wide. In stage IA2, the cancer is more than 3 but not more than 5 millimeters deep, and not more than 7 millimeters wide. A very small amount of cancer that can only be seen with a microscope is found in the tissues of the cervix. Stage IA is divided into stages IA1 and IA2, based on the size of the tumor.
Stage IB is divided into stages IB1 and IB2

In stage IB1, the cancer can only be seen with a microscope and is more than 5 mm deep or more than 7 mm wide OR the cancer can be seen without a microscope and is 4 cm or smaller. In stage IB2, the cancer is larger than 4 cm and can be seen without a microscope.

1.7.2 Stage II

In Stage II of cervical cancer, Cancer will spread beyond the cervix but not to the pelvic wall or to the lower third of the vagina. Stage II is divided into stages IIA and IIB, based on how far the cancer has spread. In stages IIA1 and IIA2, cancer will spread beyond the cervix to the vagina. In stage IIA1, the tumor can be seen without a microscope and is 4 centimeters or smaller. In stage IIA2, the tumor can be seen without a microscope and is larger than 4 centimeters. In stage IIB, cancer has spread beyond the cervix to the tissues around the uterus.
• Stage IIA: Cancer will spread beyond the cervix to the upper two thirds of the vagina but not to tissues around the uterus. Stage IIA is divided into stages IIA1 and IIA2, based on the size of the tumor.

  - In stage IIA1, the tumor can be seen without a microscope and is 4 centimeters or smaller.
  
  - In stage IIA2, the tumor can be seen without a microscope and is larger than 4 centimeters.

• Stage IIB: Cancer will spread beyond the cervix to the tissues around the uterus.

1.7.3 Stage III

In stage III, cancer will spread to the lower third of the vagina, and/or to the pelvic wall, and/or will cause kidney problems. Stage III is divided into stages IIIA and IIIB, based on how far the cancer has spread.
• Stage IIIA:

Cancer will spread to the lower third of the vagina but not to the pelvic wall.

Stage III B

In Stage IIIB of cervical cancer, Cancer will spread to the pelvic wall; and/or the tumor will become large enough to block the ureters (the tubes that connect the kidneys to the bladder). The picture shows the ureter on the right blocked by the cancer. This blockage can cause the kidney to enlarge or stop working.
1.7.4 Stage IV

In stage IV, cancer will spread to the bladder, rectum, or other parts of the body. Stage IV is divided into stages IVA and IVB, based on where the cancer is found.

Stage IVA

- Stage IVA cervical cancer. Cancer has spread to nearby organs, such as the bladder or rectum.

Stage IVB

In Stage IVB of cervical cancer, Cancer will spread to parts of the body away from the cervix, such as the liver, intestines, lungs, or bones.
1.8 Treatment for cervical cancer by stage

The stage of a cervical cancer is the most important factor in choosing treatment. However, other factors that affect this decision include the exact location of the cancer within the cervix, the type of cancer (squamous cell or adenocarcinoma), age, overall physical condition, and whether the patient wants to have children.

Stage 0 (carcinoma in situ)

Treatment options for squamous cell carcinoma in situ are the same as for other pre-cancers (dysplasia or cervical intraepithelial neoplasia [CIN]). Options include cryosurgery, laser surgery, loop electrosurgical excision procedure (LEEP/LEETZ), and cold knife conization.

For adenocarcinoma in situ, hysterectomy is usually recommended. For women who wish to have children, treatment with a cone biopsy may be an option. The cone specimen must have no cancer cells at the edges, and the patient must be
closely watched. After the woman has finished having children, a hysterectomy is recommended.

A simple hysterectomy is also an option for treatment of squamous cell carcinoma in situ, and might be done if it returns after other treatments. All cases of Carcinoma in situ (CIS) can be cured with appropriate treatment. However, precancerous changes can recur (come back) in the cervix or vagina, so it is very important for the doctor to watch the patient closely. This includes follow-up with regular Pap tests and in some instances with colposcopy.

Stage IA is divided into stage IA1 and stage IA2

**Stage IA1:** For this stage there are 3 options

- To be able to have children, first the cancer is removed with a cone biopsy, and then the patient will be watched closely to see if the cancer comes back.

- If cone biopsy doesn't remove all of the cancer (or if the family size is completed), then the uterus will be removed (hysterectomy).

- If the cancer has invaded the blood vessels or lymph vessels, it might need a radical hysterectomy along with removal of the pelvic lymph nodes. For women who still want to be able to have children, a radical trachelectomy can be done instead of the radical hysterectomy.

**Stage IA2:** There are 3 treatment options

- Radical hysterectomy along with removal of lymph nodes in the pelvis

- Brachytherapy with or without external beam radiation therapy to the pelvis
• Radical trachelectomy with removal of pelvic lymph nodes can be done if, patient still needs to be able to have children

If cancer is found in any pelvic lymph nodes during surgery, some of the lymph nodes that lie along the aorta (the large artery in the abdomen) may be removed as well. Any tissue removed at surgery will be examined in the laboratory to see if the cancer has spread further than expected. If the cancer has spread to the tissues next to the uterus (called the parametria) or to any lymph nodes, radiation therapy is usually recommended. Often chemotherapy will be given with the radiation therapy. If the pathology report says that the tumor had positive margins, this means that some cancer cells might have been left behind. This is also treated with pelvic radiation (given with cisplatin chemotherapy). The doctor may advise brachytherapy, as well.

Stage IB is divided into stage IB1 and stage IB2

**Stage IB1:** There are 3 options available:

• The standard treatment is a radical hysterectomy with removal of lymph nodes in the pelvis. Some lymph nodes from higher up in the abdomen (called para-aortic lymph nodes) are also removed to see if the cancer has spread there. If cancer cells are found in the edges of the tissues removed (positive margins) or if cancer cells are found in lymph nodes during this operation, radiation therapy may be given, possibly with chemotherapy, after surgery.

• The second treatment option is radiation with both brachytherapy and external beam radiation therapy.
- Radical trachelectomy with removal of pelvic (and some para-aortic) lymph nodes is an option if the patient still wants to be able to have children.

**Stage IB2:** There are 3 options available

- The standard treatment is the combination of chemotherapy with cisplatin and radiation therapy to the pelvis plus brachytherapy.

- Another choice is radical hysterectomy with removal of pelvic (and some para-aortic) lymph nodes. If cancer cells are found in the lymph nodes removed, or in the margins, radiation therapy may be given, possibly with chemotherapy, after surgery.

- Some doctors advise radiation given with chemotherapy (first option) followed by a hysterectomy.

**Stage II is divided into stage IIA and stage IIB**

**Stage IIA:** Treatment for this stage depends on the size of the tumor.

- One choice for treatment is brachytherapy and external radiation therapy. This is most often recommended if the tumor is larger than 4 cm (about 1½ inches). Chemotherapy with cisplatin will be given along with the radiation.

- Some experts recommend removing the uterus after the radiation therapy is done.

- If the cancer is not larger than 4 cm, it may be treated with a radical hysterectomy and removal of lymph nodes in the pelvis (and some in the para-aortic area). If the tissue removed at surgery shows cancer cells in the margins
or cancer in the lymph nodes, radiation treatment to the pelvis will be given with chemotherapy. Brachytherapy may be given as well.

Stage IIB

Combined internal and external radiation therapy is the usual treatment. The radiation is given with the chemotherapy drug cisplatin. Sometimes other chemo drugs may be given along with cisplatin.

Stage III and IVA

Combined internal and external radiation therapy given with cisplatin is the recommended treatment. If cancer has spread to the lymph nodes (especially those in the upper part of the abdomen) it can be a sign that the cancer has spread to other areas in the body. Some experts recommend checking the lymph nodes for cancer before giving radiation. One way to do this is by surgery. Another way is to do a CT or MRI scan to see how big the lymph nodes are. Lymph nodes that are bigger than usual are more likely to have cancer. Those lymph nodes can be biopsied to see if they contain cancer. If lymph nodes in the upper part of the abdomen (the para-aortic lymph nodes) are cancerous, doctors may want to do other tests to see if the cancer has spread to other parts of the body.

Stage IVB

At this stage, the cancer has spread out of the pelvis to other areas of the body. Stage IVB cervical cancer is not usually considered curable. Treatment options include radiation therapy to relieve the symptoms of cancer that has spread to the areas near the cervix or to distant sites (such as the lungs or bone). Chemo is often recommended.
Recurrent cervical cancer

Cancer that comes backs after treatment is called recurrent cancer. Cancer can come back locally (in the pelvic organs near the cervix) or come back in distant areas (spread through the lymphatic system and/or the bloodstream to organs such as the lungs or bone).

If the cancer has recurred in the pelvis only, extensive surgery (by pelvic exenteration) may be an option for some patients. This operation may successfully treat 40% to 50% of patients. Sometimes radiation or chemotherapy may be used for palliative treatment (treatment to relieve symptoms but not expected to cure). If cancer has recurred in a distant area, chemo or radiation therapy may be used to treat and relieve specific symptoms. Sometimes chemo can improve quality of life of the patients, and other times it can diminish it and the patients have to discuss this with the doctors. Fifteen percent to 25% of patients may respond at least temporarily to chemo.

New treatments that may benefit patients with distant recurrence of cervical cancer are being evaluated in clinical trials.

1.9 Prevention of Cervical Cancer

Since the most common form of cervical cancer starts with pre-cancerous changes, there are 2 ways to stop this disease from developing. One way is to find and treat pre-cancers before they become true cancers, and the other is to prevent the pre-cancers in the first place.
1.9.1 Avoiding Exposure to Human Papilloma Virus

Since HPV is the main cause of cervical cancer and pre-cancer, avoiding exposure to HPV could help prevent this disease. HPV is passed from one person to another during skin-to-skin contact with an infected area of the body. Although HPV can be spread during sex – including vaginal intercourse, anal intercourse, and oral sex – sex doesn't have to occur for the infection to spread. All that is needed is skin-to-skin contact with an area of the body infected with HPV. This means that the virus can be spread through genital-to-genital contact (without intercourse). It is even possible for a genital infection to spread through hand-to-genital contact.

Also, HPV infection seems to be able to be spread from one part of the body to another. This means that an infection may start in the cervix and then spread to the vagina and vulva. It can be very hard not to be exposed to HPV. It may be possible to prevent genital HPV infection by not allowing others to have contact with the anal or genital area, but even then there might be other ways to become infected that aren’t yet clear. In women, HPV infections occur mainly in younger women and are less common in women older than 30.

Certain types of sexual behavior increase a woman's risk of getting HPV infection, such as having sex at an early age and having many sexual partners. Women who have had many sexual partners are more likely to get infected with HPV, but a woman who has had only one sexual partner can still get infected. Waiting to have sex until you are older can help you avoid HPV. It also helps to limit the number of sexual partners and to avoid having sex with someone who has had many other sexual partners. Although the virus most often spreads between a man and a woman, HPV infection and cervical cancer are also seen in women who have only had sex.
with other women. Remember that someone can have HPV for years and still have no symptoms – it does not always cause warts or other problems. Someone can have the virus and pass it on without knowing it. Still, since all that is needed to pass HPV from one person to another is skin-to-skin contact with an area of the body infected with HPV, even never having sex doesn’t guarantee that one will not get infected. It might be possible to prevent anal and genital HPV infection by never allowing another person to have contact with those areas of body.

1.9.2 Condoms

Condoms ("rubbers") provide some protection against HPV but don't completely prevent infection. Men who use condoms are less likely to be infected with HPV and to pass it on to their female partners. One study found that when condoms are used correctly every time sex occurs they can lower the HPV infection rate by about 70%. One reason that condoms cannot protect completely is because they don't cover every possible HPV-infected area of the body, such as skin of the genital or anal area. Still, condoms provide some protection against HPV, and also protect against HIV and some other sexually transmitted diseases. Condoms (when used by the male partner) also seem to help the HPV infection and cervical pre-cancers go away faster.

1.9.3 HPV Vaccine

Vaccines have been developed that can protect women from HPV infections. So far, a vaccine that protects against HPV types 6, 11, 16 and 18 (Gardasil) and one that protects against types 16 and 18 (Cervarix) have been studied and approved for use. Both vaccines require a series of 3 injections over a 6-month period.
Side effects are usually mild. The most common one is short-term redness, swelling, and soreness at the injection site. Rarely, a young woman will faint shortly after the vaccine injection. In clinical trials, both vaccines prevented pre-cancers and cancers of the cervix caused by HPV types 16 and 18. Gardasil also prevented anal, vaginal, and vulvar cancers caused by those HPV types, as well as genital warts caused by HPV types 6 and 11. Cervarix also provides some protection against infection and pre-cancers of the cervix caused by high-risk HPV types other than HPV 16 and 18. It has also been shown to prevent anal infection with HPV types 16 and 18. Both vaccines only work to prevent HPV infection – they will not treat an infection that is already there. That is why, to be most effective, the HPV vaccine should be given before a person becomes exposed to HPV (such as through sexual activity).

1.9.4 Avoiding smoking

Avoiding smoking is another important way to reduce the risk of cervical pre-cancer and cancer.

1.9.5 HPV and men

For men, the 2 main factors influencing the risk of genital HPV infection are circumcision and the number of sexual partners. Men who are circumcised (have had the foreskin of the penis removed) have a lower chance of becoming and staying infected with HPV. Men who have not been circumcised are more likely to be infected with HPV and pass it on to their partners. The reasons for this are unclear. It may be that after circumcision the skin on the glands (of the penis) goes through changes that make it more resistant to HPV infection. Another theory is that the surface of the foreskin (which is removed by circumcision) is more easily infected by
HPV. Still, circumcision does not completely protect against HPV infection – men who are circumcised can still get HPV and pass it on to their partners.

The risk of being infected with HPV is also strongly linked to having many sexual partners (over a man's lifetime).

1.10 Cervical cancer prevention and treatment strategies in India

Non-communicable diseases including cancer are emerging as major public health problems in India. These diseases are lifestyle related, have a long latent period and need specialised infrastructure and human resources for treatment.

Cancer of the uterine cervix is still the most common cancer among women in India. Improvements in living standards and access to health care have reduced the rate of occurrence of cervical cancer in certain States like Kerala. However, the changing sexual behaviour in young adults might lead to another wave of cervical cancers. Early age at first intercourse, multiple sexual partners, poor sexual hygiene, repeated child birth etc are some of the reproductive risk factors for cervical cancer. Improvements in the living standards of women have resulted in a reduction in the incidence of cervical cancer. Regular cervical cytology examination (Pap smear) by all women who have initiated sexual activity can prevent the occurrence of cervical cancer. This has been successfully achieved in many European countries. However, there are many limitations for cytology based cervical cancer screening in India. These are various levels of health care delivery and health infrastructure in the states in India and it is possible that there are certain areas in which screening programmes could be initiated. The system for screening, with facilities for call back and proper referral, is very important, irrespective of the screening strategy.
India is the one of the few developing countries that has formulated a National Cancer Control Programme. The programme envisages control of tobacco related cancers; early diagnosis and treatment of uterine cervical cancer; and distribution of therapy services, pain relief and palliative care through augmentation of health infrastructure. Suggested surrogate outcome measures include change in tobacco use, 'Knowledge, Attitude, Practice'(KAP) pattern, compliance to screening programmes, changes in referral practices and shift in stage distribution.

1.10.1 Primary prevention and screening programs

Primary prevention is the most cost effective prevention program as it aims at reducing the incidence of cancer by risk factor modification. Fifty percent of all cancers are considered to be related to the dietary practices and the importance of a healthy diet rich in green and yellow vegetables and fruits has to be highlighted. Cancer of the uterine cervix can be controlled to a certain extent by practising genital hygiene and safe sexual practices. Cervical cytology (pap smear) screening programs were found to be successful in reducing cervical cancer incidence and women in the age group 35 to 64 years should undergo regular pap smear screening. Given the limitations in large scale population based screening programmes, India can consider primary prevention of cervical cancer by promoting genital hygiene and sexual behaviour. States that have achieved a high level of health care delivery can consider starting organised screening programmes. The primary target should be to offer once a life time screening for all women at the age of 40 years. Government and private health care providers can join in this effort and offer these services.

Measures identified and propagated for cancer control in the developed countries may not be applicable the Indian context. The answers have to be found
through methods which are feasible and evaluable in the Indian context. Cancer prevention needs to be considered as part of the Non Communicable Diseases prevention programme as it will make it more effective and feasible. The risk factors, Alcohol, Tobacco, Bad Diet and Physical inactivity are risk factors for most of the Non Communicable Diseases and have to be approached together as lifestyle modification.

1.10.2 Cancer detection & prevention clinics

Late stage at presentation is the main reason for the poor survival from cancer in India. The late presentation is mainly due to the lack of diagnostic facilities at the peripheral levels. District hospitals in India should have the services of specialists and provide reasonable services. These hospitals can have a 'Cancer Detection and Prevention Clinic', which will provide diagnostic services and minimal treatment. The diagnostic services set up in the hospital can also be of use to all the patients who attend this hospital. Cost recovery may be attempted from the beginning and an experience in Kerala has demonstrated that such services are feasible and sustainable. The services as well as the program provides a good range of services and the cytology services helped to diagnose cancers at an early stage. Provision of Palliative Care services has also been accepted by the community. Existing staff of the hospital can be trained to provide the services. Regional Cancer Centres can set up cancer detection and prevention centres in District hospitals.

1.10.3 Treatment facilities

A multidisciplinary approach to cancer treatment is essential and this has to be made available at all Regional Cancer Centres. The services of a trained surgeon and a Clinical Oncologist are needed to plan the most appropriate treatment. Radiotherapy
services are still the mainstay of treatment given the large proportion of advanced epithelial cancers in India. Given the long waiting lists and the distance that patients have to travel to reach treatment facilities, optimal strategies have to be identified. Patients for palliative treatment and curative treatment need to be identified at the beginning of the treatment plan and palliation may be achieved with the minimum time. An essential drug list has to be prepared for cancer chemotherapy and chemotherapy services for common cancers have to be made available in all centres. Advanced facilities for high intensity chemotherapy for leukaemia and other cancers where chemotherapy is the mainstay of treatment, need to be provided at the Regional Cancer Centres.

Surgical Oncology training has to be provided to General Surgeons during their training as well as to those in practice as majority of the cancers are likely to present themselves to a surgeon in the first instance.

India’s National cancer control programme emphasizes the importance of early detection and treatment. But the country has no organized screening programme, and many Indian women lack awareness about the disease and access to prevention and treatment facilities.

1.11 Innovative research on Cervical Cancer

1.11.1 Sentinel lymph node biopsy

During surgery for cervical cancer, lymph nodes in the pelvis may be removed to check for cancer spread. Instead of removing many lymph nodes, a technique called sentinel lymph node biopsy can be used to target just the few lymph nodes most likely to contain cancer. In this technique a blue dye containing a radioactive
tracer is injected into the cancer and allowed to drain into lymph nodes. Then, during surgery, the lymph nodes that contain radiation and the blue dye can be identified and removed. These are the lymph nodes most likely to contain cancer if it had spread. If these lymph nodes don’t contain cancer, the other lymph nodes don’t need to be removed. Removing fewer lymph nodes may lower the risk of later problems.

1.11.2 Targeted therapy

As researchers have learned more about the gene changes in cells that cause cancer, they have been able to develop newer drugs that specifically target these changes. These targeted drugs work differently from standard chemotherapy drugs. They often have different (and less severe) side effects. These drugs may be used alone or with more traditional chemotherapy.

1.11.3 Hyperthermia

Some research indicates that adding hyperthermia to radiation may help keep the cancer from coming back and help patients live longer. Hyperthermia is a treatment that raises the temperature in the area where the tumor is, most often by using radiofrequency antennae placed around the patient.

1.11.4 Other clinical trials

Many clinical trials are testing new chemotherapy drugs, new ways of giving radiation therapy, and new combinations of surgery and radiation therapy or chemotherapy. In 2009, the Federal Advisory Committee on Immunization Practices (ACIP) published updated recommendations for HPV vaccination in girls and young women. It recommended that females aged 11 to 12 be routinely vaccinated with the full series of 3 shots. Females as young as age 9 may also receive the HPV vaccine at
the discretion of their doctors. Women aged 13 to 26 who have not yet been vaccinated get "catch-up" vaccinations. Either vaccine may be used to prevent cervical cancers and pre-cancers. However, the ACIP recommends using Gardasil to prevent genital warts as well as cervical cancers and pre-cancers. These vaccines have been tested in women over 26, and do seem to be effective in producing an immune reaction to the HPV types in the vaccine and also reduce cervical cancers and pre-cancers in those vaccinated. But the overall benefit in this age group was small, and so they have not been approved.

1.12 Structured teaching programme

Structured teaching programme is an intervention philosophy developed by the University of North Carolina. Structured teaching is an approach to instruct the persons/people. It allows for implementation of a variety of instructional methods (e.g., visual support strategies, Picture Exchange Communication System - PECS, sensory integration strategies, etc.). Structured teaching is based upon an understanding of the unique features and characteristics. Structured teaching describes the conditions under which a person should be taught rather than "where" or "what" (i.e., "learning how to learn"). Structured teaching is a system for organizing their environments, developing appropriate activities, and helping people to understand what is expected of them.

Structured teaching utilizes visual cues which help women focus on the relevant information which can, at times, be difficult for the person. It teaching addresses challenging behaviors in a proactive manner by creating appropriate and meaningful environments that reduce the stress, anxiety and frustration which may be experienced by women. Modified behavior may occur.
Hence in the present study effectiveness of STP has been adopted to analyse the knowledge levels of women about cervical cancer.

1.13 Significance of the Study

In India a large number of female population is vulnerable to cervical cancer, since the recognized risk factors for cancer of cervix like illiteracy, low socio-economic status, early marriage, multiparty, first child birth at early age, poor genital hygiene and genital infections are widely prevalent in this population. However, the risk of development of cervical cancer is due to the life style of the individual, social customs and personal hygiene. The present study tries to analyse the socio-economic and health practices relating to knowledge of cancer of cervix among married women. However, there are few studies which focussed on the practices for prevention of the cervical cancer among women. The present study focuses on knowledge of cervical cancer, female reproductive system; symptoms and the barriers to access the health services and preventive health practices of women through structured teaching programme.

In India Cervical cancer is a major health problem among women. One of the reasons may be lack of means for early detection which forces women to often access the health services when the disease is at an advanced stage. There are a limited resources for ensuring the health care services and a stunted health care system which does not have the capacity to offer treatment for more advanced cases of cervical cancer such as radiation combined with chemotherapy. In addition to that, referral to higher recognized institutions for specialized care is difficult due to huge travel and treatment costs. Hence, knowing about the barriers to health services and interventions to improve the survival due to cervical cancer are needed.
There are certain studies relating to knowledge levels, barriers and preventive modes on cervical cancer in the Indian context. However to fill the gap, this study tries to focus on effective structured teaching program on cervical cancer among women as many women are not aware of the severity of the disease. Hence knowledge of cervical cancer through structured teaching program can make them understand and improve their decision making in health checkups.

The health problems of women are varied and they are related to the customs and beliefs, which they follow according to norms of a particular society. In order to reach the women on cervical cancer perspectives, there is a need to implement inclusive specialized policies and programs by the policy makers. An awareness programs on primary prevention can bring change in their life style, social customs and hygiene practices. So the studies, to promote preventive behavior and to prevent cancer of the cervix by detecting it at an early stage through screening are helpful in evobring the policies & programs on reproductive health and also to get the support of the family in screening.

There is a need to educate women on the importance of cervical cancer screening and of responsibilities for their own reproductive health matters as it is a critical element in fighting against cervical cancer. So, community based studies focussing on the importance of educating the women, especially, those in rural areas, are significantly important.

Hence, an attempt has been made to study the effectiveness of structured teaching program on knowledge about cervical cancer among married women in rural areas.
1.14 Chapterization of Thesis

The thesis is constructed into seven chapters -

**The first chapter** deals with introduction about the cervical cancer, its prevalence rate in developed and developing countries. Definition of Cervical cancer, risk factors, symptoms, screening, treatment and its prevention.

**The second chapter** presents a the Review of the Literature. Survey of literature is based on various articles published in the leading journals, unpublished and published books and theses submitted for presentations and newspaper and reports.

**The third chapter** focuses on the methodology and field work adopted in the study. Methodology chapter includes Research design concepts, variables of the study, hypothesis and limitations of the study, description of the setting, Sample and sampling technique, development and description of the tool, pilot study and data collection.

**The fourth chapter** deals with socio demographic variables which include; age, education, age at marriage, number of children, habits and other variables of the sample population.

**The fifth chapter** focuses on effectiveness of the structured teaching program on the knowledge about cervical cancer. It also discusses association between socio economic & demographic factors on the various issues concerning knowledge of cervical cancer.
The sixth chapter focused on Logistic Regression Analysis of the data. It is used for predicting the outcome of dependent variables based on independent variables.

The seventh chapter focused on summary and Conclusions drawn from the findings. Suggestions with suitable implications to make policies in view of the cervical cancer are also added.