



## **Incidence of colorectal cancer (CC) in patients suffering from rectal bleeding in an outpatient clinic of a hospital in Dhaka city.**

A Dissertation submitted to the Department of Pharmacy, East West University, as the Partial Fulfillment of the Requirements for the Degree of Master of Pharmacy.

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16/07/2017

## **Declaration by the Research Candidate**

I, Antor Hossain, hereby declare that this dissertation entitled “**Incidence of colorectal cancer (CC) in patients suffering from rectal bleeding in an outpatient clinic of a hospital in Dhaka city**” submitted to the Department of Pharmacy, East West University, in partial fulfillment for the requirement of the Degree of Master of Pharmacy, is an authentic research work done by me under the guidance of Professor Dr. Sufia Islam, Department of Pharmacy, East West University, Dhaka Bangladesh. The content of this dissertation in full or in parts, have not been submitted to any other Institution or University for the award of any Degree or any Diploma of Fellowship.

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## **Certificate by the Supervisor**

This is to certify that the dissertation, entitled “**Incidence of colorectal cancer (CC) in patients suffering from rectal bleeding in an outpatient clinic of a hospital in Dhaka city**” is a bona fide research work done under our guidance and supervision by Antor Hossain (ID # 2015-3-79-009), in partial fulfillment for the requirement of the Degree of the Master of Pharmacy.

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## **Certificate by the Chairperson**

This is to certify that the dissertation, entitled “**Incidence of colorectal cancer (CC) in patients suffering from rectal bleeding in an outpatient clinic of a hospital in Dhaka city**” is a bona fide research work done by Antor Hossain (ID # 2015-3-79-009), in partial fulfillment for the requirement of the Degree of the Master of Pharmacy.

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*Dedication*

*This research paper is dedicated to my  
Respected Thesis Supervisor  
&  
My beloved family*

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## **Title: Incidence of colorectal cancer (CC) in patients suffering from rectal bleeding in an outpatient clinic of a hospital in Dhaka city.**

# **ABSTRACT**

Colorectal cancer (CRC) is a malignant tumor arising from the inner wall of the large intestine or rectum. Uncontrollable division of abnormal cells occur in the colon or rectum, which ultimately form malignant tumour in patients. This type of cancer occurs in many people that are either genetically predisposed or exposed to risk factors. Rectal bleeding is a major sign of colorectal cancer. CRC is the third most common type of non skin cancer in both male and female. It is the second leading cause of cancer death in United States. Mortality is very high in patients who diagnosed with CRC at a later stage. Therefore, detection of CRC at an early stage can play a significant role before it has spread. Early detection is ultimately increase the survival rate of the patients. The objective of the study is to find out the incidence of the CC in patients suffering from rectal bleeding. Patients of sex, presenting the rectal bleeding, and visiting to a hospital in Dhaka city were enrolled in this study. Colonoscopy was done to the patients for the detection of the tumour. To confirm the malignancy, a biopsy was performed during a colonoscopy, or it may be done on any tissue that is removed during surgery. Among 26 patients, 14 patients had the history of rectal bleeding, 6 patients had abdominal pain and 7 had the history of irregular or change in bowel habit. Nine patients suffered from diarrhoea, dysentery, constipation and acidity. Seven and 6 patients had medical history of hypertension and diabetes mellitus respectively. Sixteen patients had undergone endoscopy procedure. It has been found from the endoscopy that 9 patients had no abnormality of upper GI symptoms. However, seven patients had abnormality where 3 had gastro esophageal reflux disease (GERD), 2 had duodenal ulcer and other 2 had inflammation in the lining tissue of the stomach. Colonoscopy procedure revealed that 16 patients had different types of disease in the colons. Among 16 patients who had some abnormality in colon, 2 were diagnosed with adenocarcinoma by histopathology result. Both the patients had rectal bleeding and abdominal pain. One patient had lymph node

metastases. He had history of low anterior resection for rectal cancer and colonoscopy indicated that the patient had no further growth in colon. The present study determines the risk of colorectal cancer in patients suffering from rectal bleeding in a hospital of Dhaka city, Bangladesh. Early diagnosis, symptoms indicative of a high risk of cancer are useful in order to improve survival rate of the patients.

**Key words:** rectal bleeding, colorectal cancer, colonoscopy, endoscopy, histopathology.

# **CHAPTER 01**

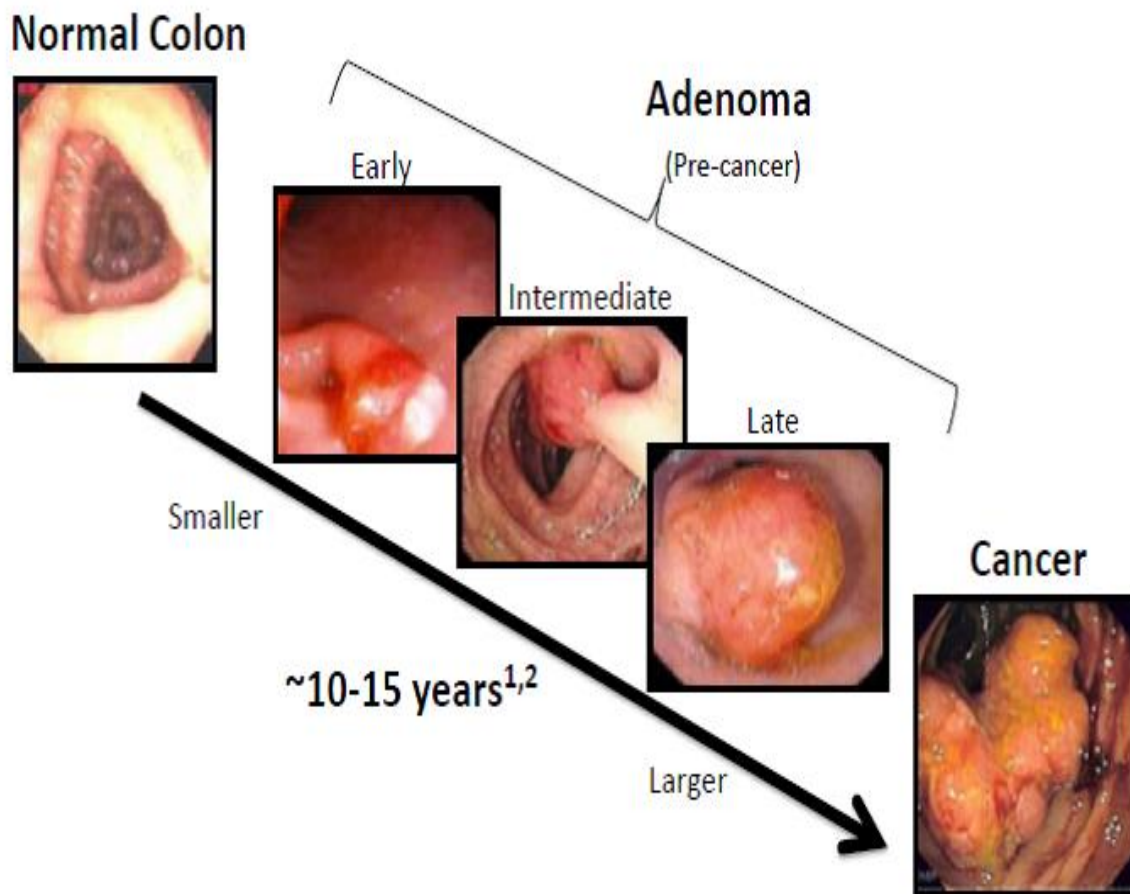
## **INTRODUCTION AND LITERATURE REVIEW**

# **Introduction**

## **1.1: Epidemiology of Colorectal Cancer**

The risk of CRC begins to increase after the age of 40 years and rises sharply at ages 50 to 55 years. CRC mortality has been declined over the last 20 years and the decline was 1.8% per year between 1985 and 2002. The overall 5 year survival rate is about 64%. If the cancer is diagnosed at Stage I, the survival rate was over 90%. The survival rate is less than 5% if the cancer is at Stage IV. According to World Health Organization (WHO) and CDC, CRC is the second most common cancer worldwide, after lung cancer. The American Cancer Society suggests that about 1 in 20 people in the US develop CRC during their lifetime. The risk is being slightly higher for men than for women. Due to advances in screening techniques and improvements in treatments, the death rate from colorectal cancer has been dropped for over 20 years (Libutti SK, 2015).

# Natural History of Colorectal Neoplasia



<sup>1</sup>Amersi et. al., Clin Colon Rectal Surg (2005)

<sup>2</sup>Zauber et. al., New Eng J Med (2012)

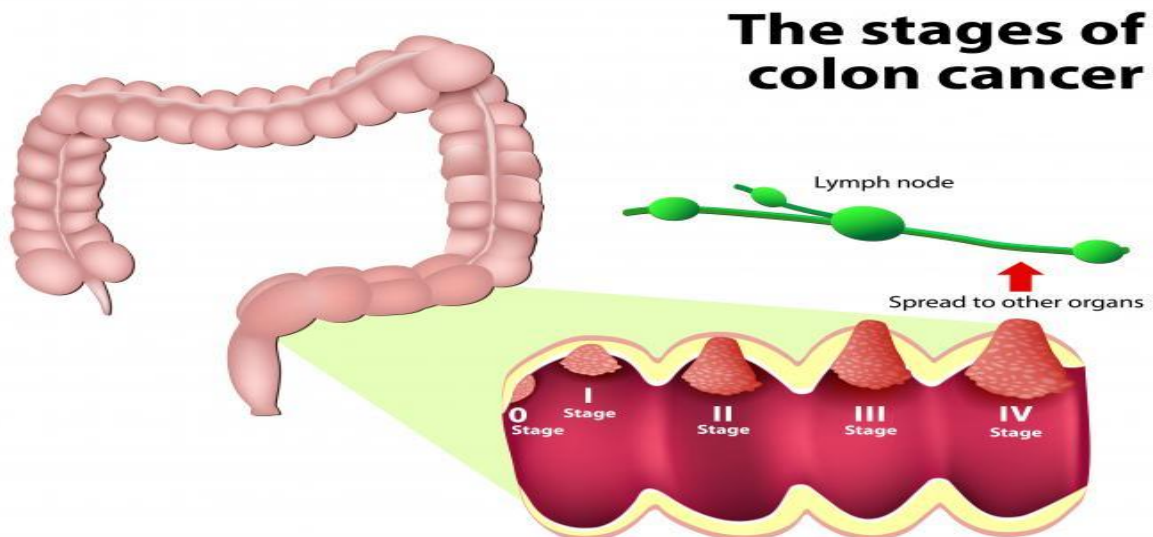
Photo source: Rozen, Young, Levin, Spann, *Colorectal Cancer in Clinical Practice* (2002)

CC - 12

**Fig 1.1: Natural history of colorectal cancer**

## 1.2 Colorectal cancer

Colorectal cancer is a cancer that starts in the colon or the rectum. These cancers can also be named colon cancer or rectal cancer, depending on where they start. Colon cancer and rectal cancer are often grouped together because they have many features in common. Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancerous, and can spread to other areas of the body. Colorectal cancer, also known as bowel cancer, colon cancer or rectal cancer is any cancer (a growth, lump, and tumor) of the colon and the rectum (American Society, 2014).



**Fig 1.2: The stage of colon cancer**

A colorectal cancer may be benign or malignant. Benign means the tumor will not spread, while a malignant tumor consists of cells that can spread to other parts of the body and damage them. The large intestine is also called the colon or large bowel. The colon and rectum belong to our body's digestive system - together they are also known as the large bowel. The colon reabsorbs large quantities of water and nutrients from undigested food products as they pass along it. The rectum is at the end of the colon and stores feces (stools, waste material) before being expelled from the body (Sigurdson ER, 2014).



### **1.2.1 Symptoms of colorectal cancer:**

- Going to the toilet more often.
- Diarrhea.
- Constipation.
- A feeling that the bowel does not empty properly after a bowel movement.
- Blood in feces (stools).
- Pains in the abdomen.
- Bloating in the abdomen.
- A feeling of fullness in the abdomen (maybe even after not eating for a while).
- Vomiting.
- Fatigue (tiredness).
- Inexplicable weight loss.
- A lump in the tummy or a lump in the back passage felt by the doctor.
- Unexplained iron deficiency in men, or in women after the menopause.

As most of these symptoms may also indicate other possible conditions, it is important that the patient sees a doctor for a proper diagnosis. Anybody who experiences some of these symptoms for four weeks should see their doctor.

### **1.2.2 Causes of colorectal cancer:**

Experts say we are not completely sure why colorectal cancer develops in some people and not in others. However, several risk factors have been identified over the years - a risk factor is something which may increase a person's chances of developing a disease or condition.

### **1.2.3 The possible risk factors for colorectal cancers are:**

- Being elderly - the older you are the higher the risk is.
- A diet that is very high in alcohol consumption.
- Women who have had breast, ovary and uterus cancers.
- A family history of colorectal cancer.

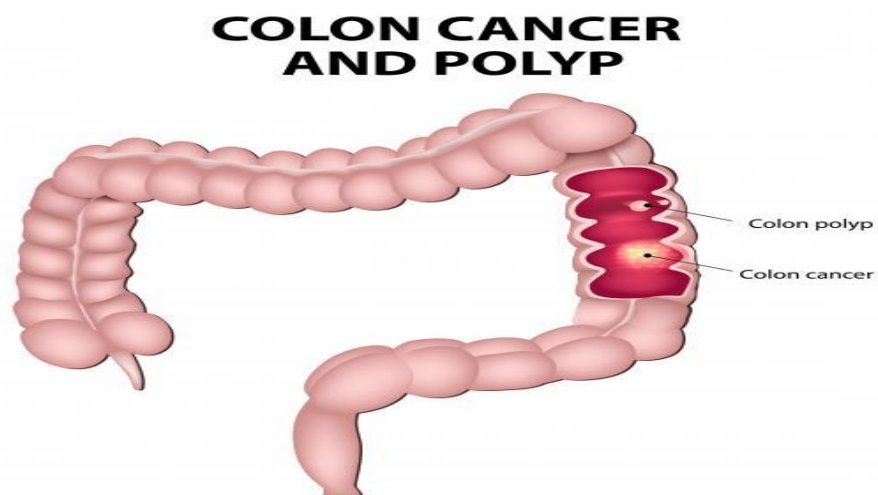
- Patients with ulcerative colitis.
- Presence of polyps in the colon/rectum. Untreated polyps may eventually become cancerous.
- Irritable Bowel Disease has a higher risk of developing colorectal cancer.

According to WHO colorectal cancer is the second most common tumor among both men and women (after lung tumors). Approximately 2% of over 50-year-olds will eventually develop colorectal cancer in Western Europe. Colorectal cancer tends to affect men and women equally. However, men tend to develop it at a younger age (Steele SR, 2013).

#### 1.2.4 Beginning of Colorectal cancer:

Most colorectal cancers begin as a growth called a *polyp* on the inner lining of the colon or rectum some types of polyps can change into cancer over the course of several years, but not all polyps become cancer. The chance of changing into a cancer depends on the kind of polyp. The 2 main types of polyps are:

1. **Adenomatous polyps (adenomas):** These polyps sometimes change into cancer. Because of this, adenomas are called a pre-cancerous condition.
2. **Hyperplastic polyps and inflammatory polyps:** These polyps are more common, but in general they are not pre-cancerous.



**Fig 1.3: Colon cancer and polyp**

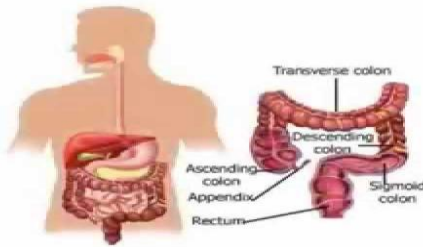
Other polyp characteristics that can increase the chances a polyp may contain cancer or increase someone's risk of developing colorectal cancer besides the type include the size (larger than 1cm), the number found (more than two), and if dysplasia is seen in the polyp after it is removed. Dysplasia, another pre-cancerous condition, is an area in a polyp or in the lining of the colon or rectum where the cells look abnormal (but not like true cancer cells). If cancer forms in a polyp, it can eventually begin to grow into the wall of the colon or rectum.

The wall of the colon and rectum is made up of several layers. Colorectal cancer starts in the innermost layer (the mucosa) and can grow outward through some or all of the other layers. When cancer cells are in the wall, they can then grow into blood vessels or lymph vessels. From there, they can travel to nearby lymph nodes or to distant parts of the body. The stage (extent of spread) of a colorectal cancer depends on how deeply it grows into the wall and if it has spread outside the colon or rectum (Van Schaeybroeck S, 2014).

### **1.3 Rectal Bleeding:**

Rectal bleeding can refer to any blood that passes from the anus, although rectal bleeding is usually assumed to refer to bleeding from the colon or rectum. Rectal bleeding may show up as blood in the stool, on the toilet paper or in the toilet bowl. Blood that results from rectal bleeding can range in color from bright red to dark maroon to a dark, tarry color. There are many possible causes for rectal bleeding and a complete evaluation and early diagnosis by the doctor is very important. Rectal bleeding should always be evaluated with a thorough consultation and examination by a physician for an accurate diagnosis and treatment plan as it may be a symptom or sign of a serious illness or condition. Rectal bleeding can be a symptom of colorectal or anal cancer, a type of cancer that can be cured if detected early. It can also be caused by hemorrhoids, anal fissures, colitis or many other causes.

# Rectal Bleeding



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**Fig 1.4: Rectal Bleeding**

Rectal bleeding often reveals itself as bright red blood on the toilet paper—usually after a bowel movement or by turning the toilet bowl water red. It can also present as extremely dark stool, ranging in color from deep red/maroon to black, and sometimes appearing tar-like (melena). The color of the blood can indicate where the bleeding is coming from:

- Bright red blood usually indicates bleeding low in the colon or rectum
- Dark red or maroon blood usually indicates bleeding higher in the colon or the small bowel
- Melena usually means bleeding in the stomach, such as bleeding from ulcers

Not all rectal bleeding is visible to the eye. In some cases, rectal bleeding can only be seen by looking at a stool sample through a microscope. There is also a test, called a Hemoccult test that can be done in a doctor's office.

## **1.3.1 Causes of Rectal Bleeding:**

Although rectal bleeding is common, only about one-third of those affected seek treatment. Symptoms usually develop quickly, and most causes are treatable and not serious. In some cases, rectal bleeding can be a symptom of a serious disease, such as colorectal cancer. Therefore, all rectal bleeding should be reported to the primary care physician. Colonoscopy is a procedure to determine the cause of the bleeding, the causes include -

- Hemorrhoids
- Anal fissure
- Anal abscess or fistula
- Diverticulitis
- Inflammatory bowel disease (IBD)
- Ulcers
- Large polyps
- Colon cancer

### **1.3.2 Symptoms associated with rectal bleeding:**

- Rectal pain and/or pressure
- Bright red blood in/on the stool, on underwear, and/or in the toilet
- Red, maroon, or black stool color
- Stool that has a tar-like appearance
- Confusion
- Feeling lightheaded or dizzy
- Fainting

### **1.3.3 Diagnosing Rectal Bleeding:**

- Examine the anus visually
- Feel for abnormalities within the rectum with a gloved, lubricated finger
- Perform a colonoscopy
- Recommend a flexible sigmoidoscopy
- Use an anoscope, a short tube with a camera on its tip.

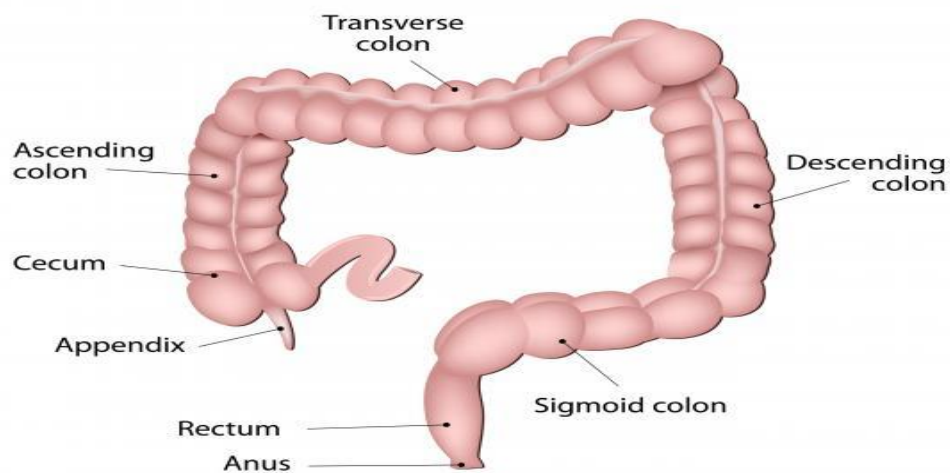
### **1.3.4 Treating Rectal Bleeding:**

Treating rectal bleeding depends on first findings its cause. It is crucial that rectal bleeding should always be evaluated with a thorough consultation and examination by an experienced NYC gastroenterologist for an accurate diagnosis and treatment plan as it may be a symptom or sign of a serious illness or condition. Rectal bleeding can be a symptom of colorectal or anal cancer, a type of cancer that can be cured if detected early. The first step is to identifying the underlying causing of rectal bleeding and determining the best treatment options (American society, 2009).

## 1.4 Cancer in the colon and rectum

The colon and rectum are parts of the digestive system, which is also called the gastrointestinal (GI) system. The colon and rectum make up the large intestine (or large bowel). Most of the large intestine is made up of the colon, a muscular tube about 5 feet long. The parts of the colon are named by which way the food matter is traveling.

### ANATOMY OF THE LARGE INTESTINE



**Fig 1.5: Anatomy of the large intestine**

The first section is called the ascending colon; it begins with a pouch called the cecum, where undigested food is received from the small intestine, and extends upward on the right side of the abdomen. The second section is called the transverse colon because it travels across the body from the right to the left side. The third section is called the descending colon because it descends (travels down) on the left side. The fourth section is called the sigmoid colon because of its “S” shape; the sigmoid colon joins the rectum, which connects to the anus (Jemal A, 2011).

The ascending and transverse sections are collectively referred to as the proximal colon, and the descending and sigmoid colon are referred to as the distal colon. The colon absorbs water and salt from the remaining food matter after it goes through the small intestine (small bowel). The waste matter that is left after going through the colon goes into the rectum, the final 6 inches of the digestive system, where it is stored until it passes out of the body through the anus.

## **1.5 Types of cancer in the colon and rectum**

Adenocarcinoma makes up more than 95% of colorectal cancers. These cancers start in cells that make mucus to lubricate the inside of the colon and rectum. Some subtypes of adenocarcinoma, such as signet ring and mucinous, may have a worse prognosis. Other, less common types of tumors can also start in the colon and rectum. These include: Carcinoid tumors start from specialized hormone-making cells in the intestine.

They are discussed in gastrointestinal stromal tumors (GISTs) start from specialized cells in the wall of the colon called the interstitial cells of Cajal. Some are non-cancerous (benign). These tumors can be found anywhere in the digestive tract, but are not common in the colon. They are discussed in Gastrointestinal Stromal Tumor (GIST).Lymphomas are cancers of immune system cells that typically start in lymph nodes, but they can also start in the colon, rectum, or other organs.

Colorectal cancer, commonly known as bowel cancer, occurs in the colon, rectum, or appendix. Genetic analysis shows that tumors in these three locations are genetically of the same cancer. Colorectal cancer is the second most commonly diagnosed cancer in females, the third in males and the fourth around the world. More than a million cases are yearly detected globally.

It is widespread in developed countries, where around 60% of the cases were diagnosed, most of which lead to death. There are several causes for the onset of colorectal cancers, which are nowadays better diagnosed and classified according to several criteria. Consistently, different treatments and prognostic measures are currently used to try and successfully cure this type of cancer (Cunningham D, 2010).

## **1.6 Causes and predisposition**

Colorectal cancer occurs in a wide range of people. Most of them were previously, and might still be exposed to numerous risk factors. The rest are either genetically predisposed, or associated with other bowel diseases.

### **1.6.1 Genetics:**

Around 18% of all cases are patients with a family history. Thus, they have a two to three-fold risk increase than other people. Furthermore, three main genetic diseases are well associated with this type of cancer. The most common is known as the Lynch syndrome, or the hereditary non polyposis colorectal cancer (HNPCC). Familial adenomatous polyposis (FAP) and Gardner syndrome are both as well strongly associated with this type of cancer.

### **1.6.2 Inflammatory Bowel Diseases:**

A third cause is the incidence of the Inflammatory Bowel Diseases, such as ulcerative colitis and Crohn's disease. The longer the onset of these diseases, and the worse the inflammation will directly affect the risk of having colorectal cancer. However, only about 2% of this cancer is associated with the previously mentioned diseases.

### **1.6.3 Pathogenesis:**

Colorectal cancer originates from the epithelial lining; most often as a consequence of mutations won't signal pathway. These mutations can be either acquired or inherited. They mostly occur in the intestinal gland stem cells.



#### **1.6.4 Tumor Suppressor Genes:**

In all colorectal cancer, APC is the most commonly mutated gene. It produces the APC protein, which prevents the accumulation of the  $\beta$ -catenin protein by binding to and degrading it. In the absence of APC protein,  $\beta$ -catenin highly accumulates in the cytoplasm, translocates to the nucleus, and binds to DNA, thus activating the transcription of several genes. These genes are responsible for stem cell renewal and differentiation. However, when improperly expressed at elevated levels they cause cancer. Some colorectal cancers have high  $\beta$ -catenin levels due to mutations in its gene CTNNB, and not in the APC gene. These mutations block the degradation of  $\beta$ -catenin. Other colorectal cancers have mutations in other APC analogues, such as NKD1, TCF7L2, AXIN1, or AXIN2. Another tumor suppressor, PTEN, normally inhibits the over expressed oncogene PI3K. However if PTEN is mutated, it becomes deactivated (Ferlay J, 2010).

#### **1.6.5 Apoptotic Proteins:**

Other than the defects mentioned above, additional mutations must take place for the cells to acquire more cancerous characteristics. One of these mutations occurs in the p53 protein, which is produced by the TP53 gene. This apoptotic protein monitors normal cell division. It kills the cells if they acquire any defect won't signaling pathway. Its mutation will change the tissue from a non-invasive adenoma into an invasive carcinoma.

In some cases, the gene encoding for BAX, another protective protein, is mutated, instead of the TP53 gene. Other apoptotic proteins are frequently mutated and deactivated in colorectal cancers. A major protein is the TGF- $\beta$ , which in at least half of colorectal cancers has a deactivating mutation. In some cases, TGF- $\beta$  is not the protein mutated, but its downstream protein SMAD. Another protein is the DCC protein, or Deleted in Colorectal Cancer. It acquires a deletion of its chromosomal segment.

#### **1.6.6 Oncogenes:**

Normal genes that encode proteins, known as oncoproteins, responsible for the regulation of cell growth and differentiation are known as proto-oncogenes. They are mainly involved in signal transduction. When activated, increased expression or mutations will result in the transformation

into oncogenes, which are tumor-inducing agents. These are over expressed in colorectal cancer, such as genes encoding the proteins PI3K, RAF, and RAS. Under normal conditions and in response to growth factors, these proteins will stimulate the cell to divide. Acquired mutations will lead to the over-activation of cell proliferation. In some cases, the chronological order of mutations is crucial for the progression of cancer. To illustrate, if at first a KRAS mutation occurred, this will lead to a self-limiting borderline lesion. On the other hand, if the KRAS mutation occurs after an APC mutation, it often leads to cancer (Merika E 2010).

### **1.7 Symptoms and diagnosis of colorectal cancer**

Signs and symptoms of colorectal cancer greatly depend on its location and ability to metastasize. These include fever, loss of appetite, weight loss, constipation, and blood in stool. In people older than fifty, common symptoms are nausea, vomiting, anemia, and rectal bleeding. It is important to note that the most evident symptoms are weight loss and rectal bleeding. Without them all other symptoms can be indicative of several different gastrointestinal diseases. Colorectal cancers occurring on the right side of the colon, i.e. the ascending colon and cecum, usually cause severe fecal obstruction and anaemia. This is because these tumors tend to grow outward from a location of the bowel wall.

However, left-sided tumors, i.e. tumors of the descending colon, cause constipation. These tumors are most likely circumferential. The first step towards diagnosis is to take tumor biopsy during wither colonoscopy or sigmoidoscopy. After confirming the presence of the cancer, imaging tests are performed of the patient's chest, abdomen and pelvis, to determine the extent of the disease. These tests include CT scan, PET, and MRI. Based on these results, the physician can establish a clear idea of the stages of the cancer, depending on the TNM system of classification.

### **1.8 Pathology of the Tumor**

After biopsy or surgery, a pathology report explicitly determines the cell type and grade of the tumor. In 95% of the cases, the colon cancer type is adenocarcinoma. It originates from the glandular epithelium, invading the wall and infiltrating all layers. Tumor cells have irregular structures and might secrete mucus.

Depending on the predominant cellular pleomorphism, gland architecture, and secretion of mucus, adenocarcinoma is separated into three differentiation levels poorly, moderately, and well differentiated. Other than adenocarcinoma, rare types of colorectal cancer include squamous cell carcinoma and lymphoma. Besides, the majority of colorectal cancer tumors are cyclooxygenase-2, or COX-2, positive. This enzyme is abundantly found in cancerous tissue of the colon. It aids in abnormal cell growth (Watson AJ 2011).

## **1.9 Treatment and prognosis**

As any other type of cancer, the treatment of colorectal cancer depends on its advancement. At early stages, surgery is mostly curative. At later stages when the cancer is metastatic, physicians tend to treat their patients by trying to prolong their life and keep them comfortable.

### **1.9.1 Surgery:**

Patients with localized colorectal cancer undergo surgeries to extract the tumor. It is either done by laparotomy or laparoscopy, which is a minimally invasive procedure. If other tumors are metastasized to the lungs or liver, they are removed surgically.

### **1.9.2 Chemotherapy:**

In some cases, chemotherapy is used before surgery. This will help shrink the tumor before eradicating it. In other cases where the cancer has metastasized and entered the lymph nodes, chemotherapy is a must to help increase the life expectancy of the patient. Drugs may include oxaliplatin, irinotecan, leucovorin, UFT, capecitabine, or 5-fluorouracil. Monoclonal antibodies against molecular targets include cetuximab, panitumumab or bevacizumab.

Understanding better the tumor biology and molecular pathways and mechanisms effectively led to the discovery of novel agents that specifically target molecular elements of cancer cells. This has helped improving the efficacy of drug-based chemotherapy that is nowadays combined with targeted monoclonal antibodies. Research is being extensively done to try and use cell signaling pathways as targets for colorectal cancer treatment, even though these pathways highly intercorrelate and crosstalk.

### **1.9.3 Radiation:**

Combining chemotherapy and radiation might be helpful. But, in most cases, this is not used as curative technique, since the bowels are highly sensitive to radiation.

### **1.9.4 Palliative Care:**

At the stage when colorectal cancer becomes incurable, the best remedy is to improve the quality of life by alleviating the symptoms and reducing the complications. These procedures may include stent placement or bypassing part of the intestine, and pain medications. This will help reduce bleeding, intestinal obstruction, and abdominal pain. Survival rates are directly linked to the type of cancer and its detection. Late stage cancers have five times less survival rates than early stage ones. To be on a safe side, follow-up is highly mandatory. This will help diagnose any new tumors that develop later, but had not originated from the original tumor. Physical examinations are recommended, as well as blood tests and CT scans.

## **1.10 Prevention**

The most important ways to prevent colorectal cancer are a healthy lifestyle, appropriate medication, and continuous screening.

### **1.10.1 Life Style:**

Dietary recommendations include reducing the consumption of red meat and increasing the intake of fruits, vegetables, fibers and whole grains. Physical activity also helps reducing the risk of colorectal cancer.

### **1.10.2 Medication:**

People at high risk of having colorectal cancer are advised to take aspirin and celecoxib. They both appear to decrease the risk factor. Nevertheless, these drugs are not recommended to those at average risk. Vitamin D, especially its blood concentration, and Calcium intake are also associated with lower risks of colorectal cancer.

### **1.10.3 Screening:**

Several screening methods are applied nowadays, and they proved to be helpful in reducing death by the early detection. The three main tests are fecal occult blood testing of the stool, sigmoidoscopy, and colonoscopy. The newest screening method is the M2-PK test to stool samples. The M2-PK enzyme biomarker is highly sensitive to colorectal cancer (FedirkoV, 2011).

## **1.11 Hemorrhoids and most common cause of rectal bleeding**

Hemorrhoids are swollen veins in the rectum (internal hemorrhoids) or the anus (external hemorrhoids). Hemorrhoids, also called piles, can commonly develop because of chronic constipation or straining at stools, pregnancy, work strain (heavy lifting, etc.), obesity, or anal intercourse. Hemorrhoid treatment includes addressing the underlying causes, such as treating the constipation or straining habits, or changing work habits if necessary. Sometimes surgical treatment is necessary and may include one of the following methods:

- Rubber band ligation: a rubber band placed around the base of the hemorrhoid cuts off circulation to the bulk of the hemorrhoid and causes the hemorrhoid to wither away.
- Sclerotherapy: the injection of a chemical solution around the blood vessel shrinks the hemorrhoid.
- Laser: a precise laser beam is used to burn away small hemorrhoids.
- Hemorrhoidal arterial ligation: uses a Doppler probe to locate and tie the blood vessels feeding the hemorrhoid, to shrink it.
- Procedure for prolapsed hemorrhoids (PPH): puts hemorrhoids that have come out of the anal canal back in their original positions.
- Hemorrhoidectomy: surgical removal of the hemorrhoid.

### **1.11.1 Anal Fissure:**

An anal fissure, a split or tear in the lining of the anus, causes bleeding and burning pain after bowel movements. The usual cause is passing a very hard stool. The pain is caused by a spasm of the sphincter muscle. This happens as a protective measure by the body as stool passes through and expands the tear. Bleeding is result of trauma to the existing tear. Fissures may be mistaken for and misdiagnosed as hemorrhoids. Fissures often improve by themselves, but if they don't, an

ointment or medication applied locally to relax the muscle can relieve the pain (Valori R, 2010). Surgery may be needed for a chronic or recurrent fissure or if excessive sphincter spasms prevent the tear from healing on its own.

### **1.11.2 Perianal Abscess:**

There are small glands that open inside the anus, believed to help with passing stool. An infection can occur when one of these glands becomes blocked. The pocket of pus that results from the blockage is an abscess. The abscess can be drained under local anesthesia in the doctor's office. Large abscesses need drainage under anesthesia. About a third of all perianal abscesses will develop into an anal fistula.

### **1.11.3 Fistula:**

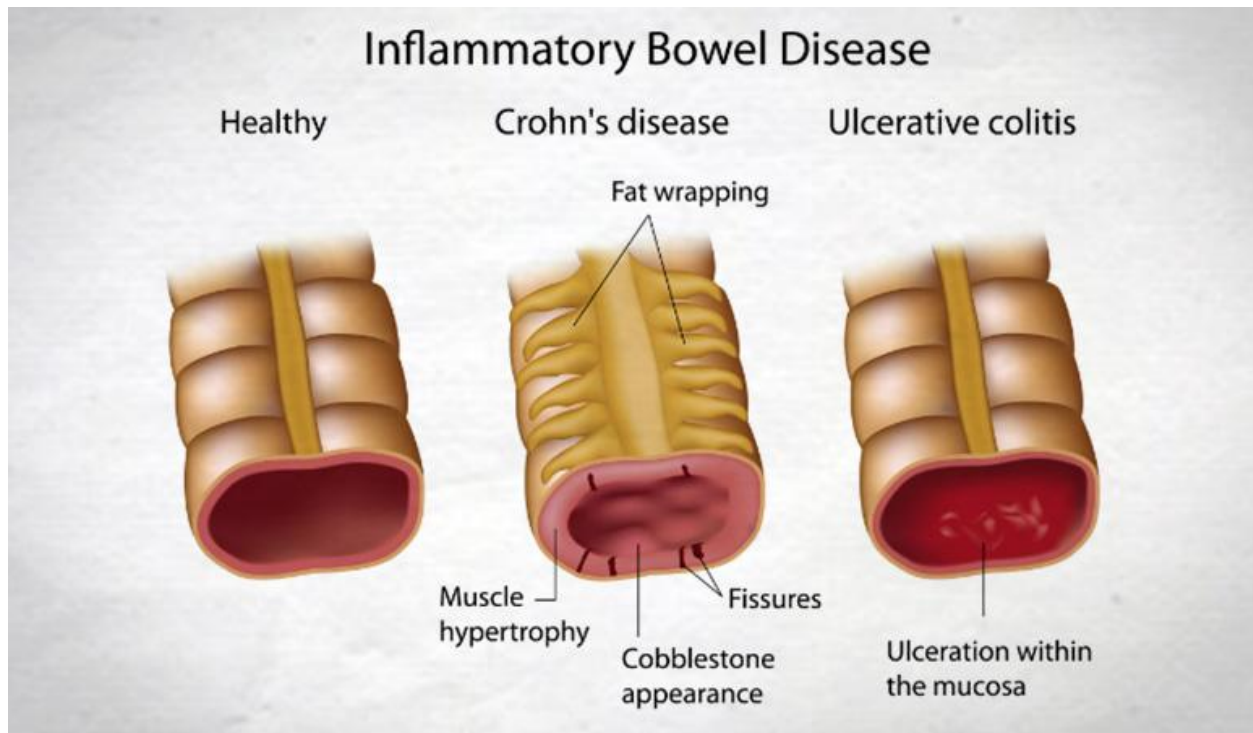
An anal fistula is a consequence of an infection in the perianal area. A fistula is a connection between two spaces. An anal fistula is a connection between the anus and rectum to the skin around the anus. Fistulas usually start as infections in the anal gland that is naturally present in the anus. They require surgery in order to heal. Some anal fistulas have other causes like inflammatory bowel disease, tuberculosis, or radiation. Others can result from surgery in that area.

### **1.11.4 Diverticulosis and diverticulitis:**

Diverticulosis develops when small pouches (diverticuli) form in weakened sections of intestine lining and protrude through the bowel wall, usually in the sigmoid colon. Diverticuli are a common finding among older people in Western societies and are diagnosed when seen on a colonoscopy or sigmoidoscopy. Diverticulosis is a benign disorder but bleeding and infection can occur and are associated complications. Diverticuli generally occur without symptoms, unless they become blocked and infected, causing diverticulitis. Symptoms of diverticulitis include abdominal pain, fever, and a sudden change in bowel habits. Treatment may include a special diet, antibiotics, or surgery (Denis B, 2011).

### 1.11.5 Inflammatory bowel disease (IBD):

Inflammatory bowel disease (IBD) is an inflammation of the small or large intestine. There are two types of IBD. One type of IBD is Crohn's disease, marked by patches of inflammation occurring anywhere in the digestive tract. The other type of IBD, colitis, is marked by inflammation in the large bowel.



**Fig 1.6: Inflammatory bowel disease**

**There are several other types of colitis, including:**

- Infectious colitis (caused by an infection that attacks the large bowel)
- Ischemic colitis (the result of a poor blood supply to the colon)
- Radiation colitis (following radiotherapy, usually for prostate, rectal, or gynecological cancer)
- Ulcerative colitis (ulcers/sores in the large intestine lining)

**IBD symptoms may include:**

- Fever

- Rectal bleeding
- Diarrhea
- Abdominal pain and/or cramping
- Intestinal blockage

Treatment of inflammatory bowel disease is critical and may involve a special diet, medication to eliminate or reduce inflammation, and/or surgery.

#### **1.11.6 Ulcers:**

Ulcers are sores in the stomach lining or in the first section of the small intestine (the duodenum,) caused by an imbalance of digestive fluids in the stomach and the duodenum. While abdominal pain is the most common symptom of ulcers, many ulcers produce no obvious symptoms. Ulcers that bleed into the gastrointestinal tract may cause black stool, sometimes with a tar-like appearance. Ulcers are usually successfully treated without surgery, and successful treatment may also prevent new ulcers from forming (Siegel R, 2008). Treatment methods may include:

- Special diet
- Antibiotics
- Medications that neutralize gastric acid, or reduce the secretion of gastric acid
- Medications that strengthen gastric acid resistance in the stomach and the duodenum

#### **1.12 Polyps and polyps related to colorectal cancer**

Since rectal bleeding can sometimes be a symptom of colorectal cancer – cancer of the colon or rectum – this is the primary reason rectal bleeding should not be ignored. Colorectal cancer is a common form of cancer that can usually be cured if diagnosed and treated early enough.

Colorectal cancer occurs when the normal growth and division of the cells lining the large bowel goes out of control, initially resulting in the formation of a polyp(s). A polyp can appear similar to a small mushroom that is attached to the lining of the large bowel. Polyps that become large can bleed. While there are many types of polyps that are not cancerous, certain polyps are



considered precancerous and can develop into cancer if left untreated. Therefore, removing polyps before they develop such severe changes can prevent cancer.

Colonoscopy is the procedure used by physicians to locate and remove polyps to prevent colorectal cancer. People having an increased risk of colorectal cancer include those who have a family history of colorectal cancer, and people who have previously had cancer or polyps. When colorectal cancer occurs, treatment may include:

- Surgery
- Chemotherapy
- Radiation treatment

The early stages of colorectal cancer may have no apparent symptoms. Thus, regular screening is important, particularly for individuals who are at increased risk.

### **1.12.1 Colon Cancer:**

More serious causes of rectal bleeding are a colon cancer. The second leading cause of cancer deaths in the United States, colon cancer begins in the large intestine. Since it is a slow-growing disease, it can be effectively treated with early detection. Most cases of colon cancer come from polyps in the colon. Finding polyps through a colonoscopy and removing them reduces the cancer risk. Anal cancer is less common but also curable when diagnosed early.

### **1.12.2 Hemorrhoids:**

Hemorrhoids are veins just below the surface of the skin that have become inflamed or swollen. They can occur on the skin around the anus (external hemorrhoids) or inside the rectum (internal hemorrhoids). Already sensitive, they can bleed easily if irritated. Common causes of hemorrhoids are:

- Sitting on the toilet too long
- Straining during bowel movements
- Aging
- Chronic diarrhea or constipation

- Pregnancy
- Obesity
- A low-fiber diet

### **1.12.3 Colon Polyps:**

Rectal bleeding can be caused by an abnormal, benign cell growth. Colon or rectal polyps are benign growths within the lining of the colon or rectum. Some can cause minor bleeding. Polyps usually are the result of abnormal cell growth. Although a vast majority of polyps do not lead to cancer, some do if left untreated, so it's important to remove them. That's why most doctors recommend a regular colonoscopy for people over 50 (Ries L, 1997-2004).

### **1.12.4 Proctitis:**

Proctitis is a medical condition that occurs when the lining of the rectum and rectal lining becomes inflamed. This can be a painful condition. Symptom of proctitis can include a bleeding from the rectum (Joe V, 2011).

#### **Causes include:**

- An infection
- Certain medications
- Prior radiation therapy for cancer treatment
- Some forms of inflammatory bowel disease (IBD)

## **1.13 Literature Search**

Colorectal cancer (CRC) is a major public health problem throughout the world. According to the World Health Organization (WHO) and CDC, CRC is the second most common cancer. It is the second leading cause of cancer death in United States (Howlader N, 2015). Rectal bleeding may be associated with this which is considered as a major symptom of CRC. However, the symptom of bleeding is infrequently reported to the general practitioner (Pedersen AF, 2013). The associated risk factors of CRC include age (over 50 years), consumption of high fat diet, daily alcohol use, sedentary life style, obesity, history of polyps etc. Mortality is very high in patients who diagnosed with CRC at a later stage (Robertson R, 2006).

Although there is advancement in the screening procedure of CRC and the use of chemotherapeutic agents, metastasis is developed in approximately 50% of the CRC patients (Kindler H, 2001). According to the American Joint Committee on Cancer staging system, advanced stage is defined as stage III, whereas stage IV is defined as distant metastasis (Corley D, 2014). Colonoscopy is an important tool for diagnosis of colorectal cancer and polyps (Uraoka, T, 2015). A significant increase in MiR-92 in plasma has been found in CRC patients when compared with the healthy control. This marker was significantly reduced after the surgical intervention in 10 patients, thus a potential noninvasive diagnostic tool for CRC screening (Ng EK, 2009). It has been reported from a study that one in ten patients with new onset of rectal bleeding had either CRC or colonic adenoma. In this study among 265 patients aged 45 years or above, 15 patients have colorectal cancer, 13 patients were diagnosed with colonic adenoma during 10 year period in a rural general practice in the United Kingdom (du Toit, 2006). Polyps begin in the cells of glandular structures lining the colon. Most polyps are benign; however, Colon Adenomatous Polyp is the cause of greater concern. The growth is associated with DNA changes in the lining of the colon. Up to 10% of these polyps can become cancerous within a 10 year period if undetected or ignored. Another study showed that among 208 patients aged 40 and above with rectal bleeding, 15.4% found to have CRC and 7.7% have polyps. It has been also shown from the same study that 156 patients reported first episode of rectal bleeding or changes in their usual bleeding pattern. Among them 21 patients had CRC (Nørrelund N, 1996). An observational study on patients with rectal bleeding was carried out in primary care setting in southern England. Twenty two patients were diagnosed with CRC out of 604. The significant predictors for CRC in these patients were age more than 50 years and blood mixed with stool. Patients with haemorrhoid along with bright red bleeding which is not mixed with stool reduced likelihood of colorectal cancer (CRC). However, it cannot be eliminated because 2% patients had CRC with these symptoms as well (Robertson R, 2006). A prospective study was carried out on 99 patients aged over 40 years presenting with rectal bleeding. Serious pathology was detected by colonoscopy in 44.4% of patients. Colorectal carcinoma was diagnosed in 8 patients. Polyps, inflammatory bowel disease, diverticular disease and hemorrhoids were found in 25, 11, 16 and 28 patients respectively (Metcalf J. V., 1996).

A study in Belgium showed that among 386 patients with rectal bleeding, 27 had colorectal cancer. Associated sign and symptoms were recorded as fatigue, weight loss, pain and palpable rectal tumour. The study also reported that the positive predictive value was increased with the age of the patients (Wauters H, 2000).

So far to our knowledge no study has been carried out in Bangladesh to find out the incidence of colorectal cancer from patients suffering from rectal bleeding. In Bangladesh perspective this study is very important to know the incidence of the disease along with the age group and sex of patients suffering from CRC.

# **CHAPTER 02**

## **OBJECTIVES**

## 2.1 Research objectives

- ❖ To determine the incidence of colorectal cancer (CRC) in patients suffering from rectal bleeding visited in an outpatient department of a hospital in Dhaka city.
- ❖ To determine the age group and sex of the patients suffering from rectal bleeding and diagnosed as colorectal cancer (CRC).
- ❖ To find out the possible risk factors of colorectal cancer (CRC).

# **CHAPTER 03**

## **METHODOLOGY**

### 3.1 Methods

Patients of sex, presenting the rectal bleeding, and visiting to the hospital were enrolled in this study. A complete history and physical examination of the patient was done by the physician. Symptoms of the patient, such as, changes in bowel habits, colour and consistency of the stools, the presence of pain and tenderness were recorded by the physician. The patients were advised to come in empty stomach before the endoscopy and colonoscopy. A consent form was given to the patient prior to the procedures. Xylocaine throat spray and 1.5 mg Midazolam were given to the patients before the endoscopy.

The endoscopy was performed to the patients for upper gastrointestinal symptoms. A mouthpiece was put in the mouth and the endoscope was inserted through the mouthpiece and down to the esophagus, stomach and duodenum. This procedure took about 5 minutes. Then the patients were given 50 to 100 mcg fentanyl opiate and further 1.5 mg Midazolam for colonoscopy procedure. It took few minutes to start colonoscopy after the end of gastrocopy. This procedure took between 15 to 45 minutes depending on the patient's condition.

This procedure is used as a common or primary detection tool for the patients with abnormal growth in colon and rectum. Sample of the tissue was collected if abnormality was detected for histopathology to confirm the disease. After signing the consent form the patients were undergone the endoscopic procedure for the upper gastrointestinal symptoms. A mouthpiece was put in the mouth and the endoscope was inserted through the mouthpiece and down to the esophagus, stomach and duodenum. After the procedure which takes about 20 minutes, the patients were advised to take rest and ready for the next procedure. Then the colonoscopy was performed that allowed the specialist to detect the area of the large intestine and examine the bleeding area.

The colonoscopy is used as a common or primary detection tool for the patients with abnormal growth in colon and rectum. Sample of the tissue was collected if abnormality was detected for further biopsies. The patients diagnosed with colon tumors were advised for further testing to confirm the disease. Patients with hemorrhoids, anal fissure, infection, inflammation (ulcerative colitis), colorectal polyps, colon cancer and diverticular disease were advised to come to the



hospital with an empty colon. This test was performed to examine the rectum and the entire colon by using a colonoscopy. During the procedure any abnormal growth in colon and the rectum can be removed.

### 3.2 Preparing for a Colonoscopy

A colonoscopy is a test in which a flexible tube, about the thickness of the index finger, with a small camera (a colonoscopy) is inserted in the rectum. The camera is connected to a display monitor, which allows the doctor to see and examine the inside of colon (large bowel).



**Fig 3.1: Procedure of Colonoscopy**

### 3.3 Recommended of a Colonoscopy

Cancer of the colon usually starts from a polyp. A polyp is a wart-like growth of cells. Although most polyps are benign (not cancerous), removing them is an important way of preventing colon and rectal cancer. If polyps are found during the colonoscopy, most of them should be removed. The procedure to remove polyps is called a polypectomy. Polyps are removed by burning them off or by placing a wire snare around their base and applying to it an electric current. The sample is then sent to the lab for testing.



**Fig 3.2: Colon Cancer and Polyp**

There is a small chance that the doctor might miss a polyp or cancer. Out of 100 patients with cancer, up to 15 cases may not have been diagnosed during a previous colonoscopy (within 6-36 months prior). Alternatives to a colonoscopy are limited if the patients have gastro-intestinal symptoms, a positive stool test, or a personal or family history of polyp or colorectal cancer. For screening purposes, there are other tests that can be done instead of a colonoscopy but a colonoscopy has the advantage of allowing tissue samples to be taken (biopsy) and polyps to be removed. The other screening tests do not. Other options for screening include:

- Stool tests: fecal occult blood test (FOBT) and fecal DNA
- CT colography scan (commonly known as a virtual colonoscopy, which also requires a bowel preparation).

### **3.4 During the Test**

During the test, patients may feel some discomfort (pain, bloating or cramps), which is normal. These symptoms may last after the test and usually improve over the next few hours. Patients may receive a medication (sedation) to relax and control the pain or discomfort. The test takes between 15 to 30 minutes to be completed, but the patients should be expected to spend between 1 ½ hours to 3 hours at the hospital.

### **3.5 After the Test**

Once the test is over, the patient is taken to the recovery room, where the nurses continue to monitor until the sedation wears off. Recovery can take 30-45 minutes.



Fig 3.3: No Alcohol and Smoking

### 3.6 Possible complications

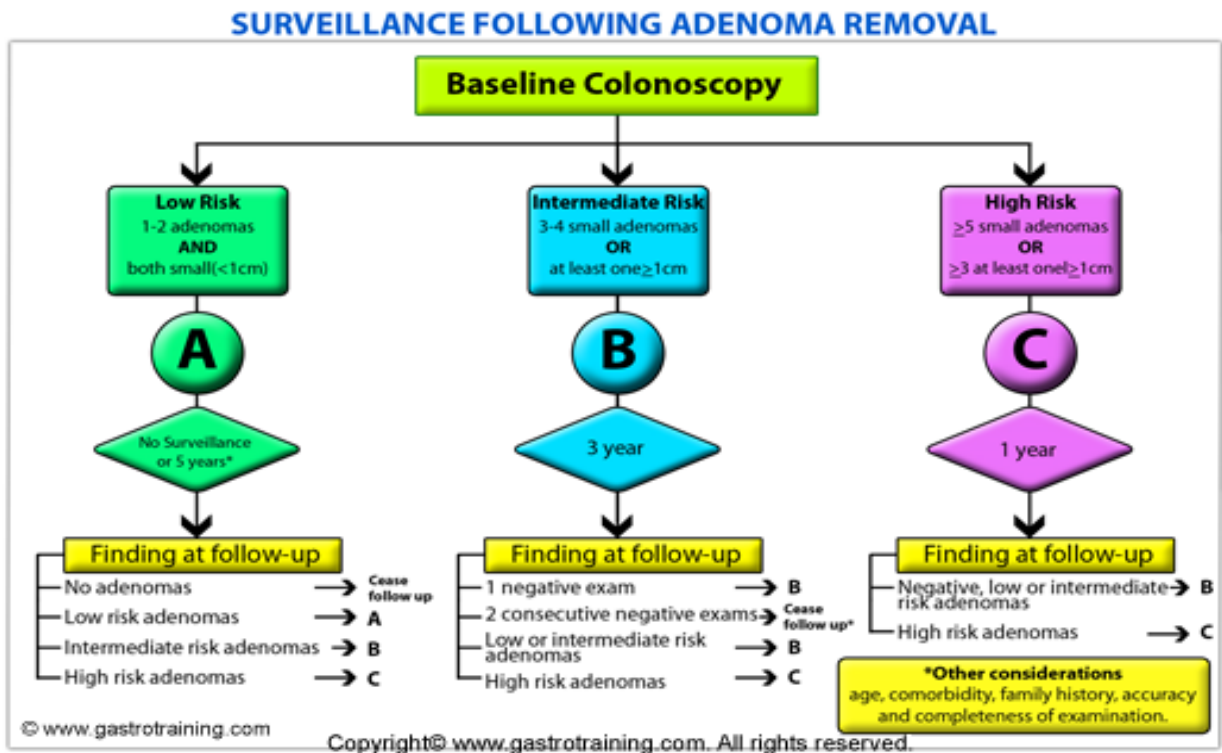
Complications can happen but they are rare.

**Perforation:** There is a chance that patient could get a tear or hole in the wall of the colon. If this does happen, intravenous antibiotics are given and possibly have a surgery. The risk of perforation ranges from less than 1 in 5000 for screening colonoscopies to less than 1 in 1000 for non-screening colonoscopies. The risk of perforation can be higher if a polypectomy is performed than if a polypectomy is not performed.

**Bleeding:** Bleeding may occur after a biopsy and or a polyp is removed. It is usually minor and stops on its own or it can be controlled by special techniques during the colonoscopy. The risk of bleeding ranges from less than 1.6 in 1000 to less than 1 in 100 depending on whether a polypectomy is performed. If the bleeding is extensive, a blood transfusion may be necessary and a colonoscopy may be repeated.

### 3.7 Method of Colonoscopy

Colonoscopy is fundamental to the diagnosis and management of digestive diseases and plays a key role in colorectal cancer (CRC) screening and diagnosis. Therefore, it is important to ensure that colonoscopy is of high quality.



**Fig 3.4: Baseline of Colonoscopy**

During a colonoscopy, doctor uses a thin, flexible camera to check for abnormalities or disease in lower intestine or colon. The colon is the lowest portion of the gastrointestinal tract that takes in food, absorbs nutrients, and disposes of waste. The colon is attached to the anus via the rectum. The anus is the opening in the body where feces are expelled. During a colonoscopy, the doctor may also take tissue samples for biopsy. They may also remove abnormal tissue such as polyps.



**Fig 3.5: Process of Colonoscopy**

A colonoscopy can be done as a screening for colon cancer and other problems. The screening can help the doctor:

- Look for signs of cancers and other problems
- Explore the cause of unexplained changes in bowel habits
- Evaluate symptoms of pain or bleeding located in the abdominal area
- Find a reason for weight loss, chronic constipation, or diarrhea

Everyone over the age of 50 who is at average risk of colon cancer should get a colonoscopy once every 10 years.

During the procedure, the patient lies on the side on a padded examination table. The doctor may position the patient with knees close to chest to get a better angle to the colon. While patient is on his/her side and sedated, the doctor guide a flexible, lighted tube called a colonoscopy into the anus. Slowly and gently, they'll guide it up through the rectum and into the colon. A camera on the end of the colonoscopy transmits images to a monitor that the doctor will be watching. Once the scope is positioned, doctor will inflate the colon using carbon dioxide gas. This gives them a

better view. The doctor may remove polyps or a tissue sample for biopsy during this procedure. The entire procedure takes about 40 minutes to an hour (Colorectal 2014).

### **3.8 Risks of a Colonoscopy**

Since a colonoscopy is a routine procedure, there are typically few lasting effects from this test. In the vast majority of cases, the benefits of detecting problems. And beginning treatment far outweighs the risks of complications from a colonoscopy. Some rare complications include:

- Bleeding from a biopsy site if a biopsy was done
- A reaction to the sedative
- A tear in the rectal wall or colon

### **3.9 Colonoscopy Technique**

A long, flexible, lighted viewing tube (colonoscopy) is inserted through the rectum into the colon. The scope is advanced and maneuvered while the lumen and walls of the colon are visualized by means of projections onto a television screen. The colonoscopy has channels through which instruments can be passed in order to perform biopsies, remove polyps, or cauterize bleeding. Air, water, and suction can be applied to help provide a clearer visual field for inspection. Of patients with colorectal cancer, has a second synchronous tumor, and 27-53% has concomitant multiple adenomatous polyps. For this reason, a complete examination should be performed during colonoscopy.

The goal for a complete examination is to reach the cecum and, in some cases, the terminal ileum. Landmarks that may help in determining whether this has been achieved include visualization of the appendiceal orifice and the ileocecal valve. Tran illumination above the right inguinal canal also suggests cecal intubation. Full inspection from the rectum through the cecum is not always possible. For example, stenosing tumors, acute diverticulitis, adhesions from previous pelvic surgery, post radiation stenosis, in some cases, a double-contrast barium enema is necessary to complete an examination, though this procedure is less sensitive than colonoscopy in detecting tumors and polyps (ACR Practice, 2009).

### **3.10 Additional Considerations**

The alternative use of pediatric colonoscopes in adults has been studied. (Pediatric colonoscopes are thinner, more flexible, and generally shorter.) Employment of a pediatric colonoscope was found to be as successful as use of adult colonoscopes in performance of total colonoscopy in all outcome measures, including frequency of reaching the cecum, time needed to reach the cecum, total procedure time, endoscopists' perception of procedure difficulty, patients' assessment of comfort, and likelihood of need for a repeat examination in the future. Whether particular subgroups exist for whom the use of pediatric colonoscopes actually has an advantage over the use of adult colonoscopes remains to be determined. Investigators have also looked into colonoscopic withdrawal technique. A study by Rex associated higher-quality withdrawal techniques with lower miss rates for adenomas (Rex DK, 2000). In view of the findings, it has been suggested that withdrawal technique should be subjected to further study and that standards for these techniques should be developed. Colonoscopy technique must be modified in a pregnant woman. To avoid uterine trauma, only minimal, if any, compression should be placed on the abdomen. Similarly, even if the study is difficult, pregnant women should never be placed in a prone position, as may be done with nonpregnant patients. If the study is so difficult that this maneuver becomes necessary, the procedure should be stopped. Moreover, if sedation is to be used, diazepam should be avoided because of unconfirmed reports of teratogenicity. (Meperidine has a better-documented fetal safety profile than midazolam does.) Fetal cardiac monitoring during the procedure should also be considered.

### **3.11 Alternative Approaches to Colonoscopy**

#### **3.11.1 Virtual colonoscopy:**

Virtual colonoscopy, also known as computed tomography (CT) colography, refers to the use of spiral CT and computers to simulate colonoscopy by generating high-resolution multidimensional views of the colon. As with traditional colonoscopy, the bowel must be prepared and cleared before the study. At the time of the CT scan, a rectal tube is inserted and the colon is filled with air. Intravenous glucagon may be used to relax the smooth muscle. Spiral CT is then performed (without any need for contrast), and a specialized computer is used to process the images obtained.

Virtual colonoscopy is less invasive than traditional colonoscopy and has the potential to be more accurate in determining the size, shape, and location of lesions. Suggested indications for this method include detection of polyps and carcinomas and staging of cancers. Some researchers have even suggested the possibility of someday being able to make tissue diagnoses on the basis of certain numerical values. Disadvantages include increased cost, possible increased discomfort (patients complain of more pain and discomfort during virtual colonoscopy than during endoscopic colonoscopy with conscious sedation), poor sensitivity for small polyps, and inability to accomplish biopsy or polyp removal, thus necessitating additional studies (Johnson CD, 2008). Still in the investigational stages are faster scanners with increased resolution and capabilities. Researchers suggest the possibility of oral labeling agents that may eliminate the need for bowel cleansing. In addition, computer-aided polyp detection systems as an adjunct to virtual colonoscopy are being studied for their ability to increase sensitivity for smaller polyps. Virtual colonoscopy holds promise as a safe and relatively noninvasive addition to the future of colon imaging.

### **3.11.2 High-definition Colonoscopy**

High-definition colonoscopy may provide better detection of colorectal polyps than traditional colonoscopy does. In a retrospective study, Buchner et al compared high-definition colonoscopy with standard white-light colonoscopy for the detection of adenomas. The investigators found that the adenoma detection rate and the polyp detection rate were higher among patients, who underwent high-definition colonoscopy, which they concluded could reduce the number of missed adenomas and the subsequent risk for colorectal cancer.

Tribonias et al also found no significant differences between high-definition, wide-angle endoscope and standard colonoscopy for the detection rate of adenomas and hyperplastic polyps; large, medium, and small adenomas; and large and medium-sized hyperplastic polyps.

### **3.11.3 Double-balloon Enteroscopy**

The small bowel has previously been one of the most endoscopically inaccessible areas of the gastrointestinal (GI) tract, with access limited by the distance achievable by using an enteroscope. Most diagnosis and treatment of lesions within the small bowel required open



surgery. Double-balloon enteroscopy, a method developed by Yamamoto et al, not only enables exploration of the entire small bowel but also allows for interventional therapy, including biopsies, hemostasis, polypectomy, and tattooing.

The double-balloon enteroscope has two balloons, one at the tip of the endoscope and the other on a transparent tube passing over the endoscope. Sequential inflation and deflation of these balloons as the endoscope is advanced allows for pleating of the bowel over the scope and forward movement through the small intestine. It can be used from either an oral (upper endoscopy) insertion or an anal (colonoscopy) insertion (Halligan S, 2011).

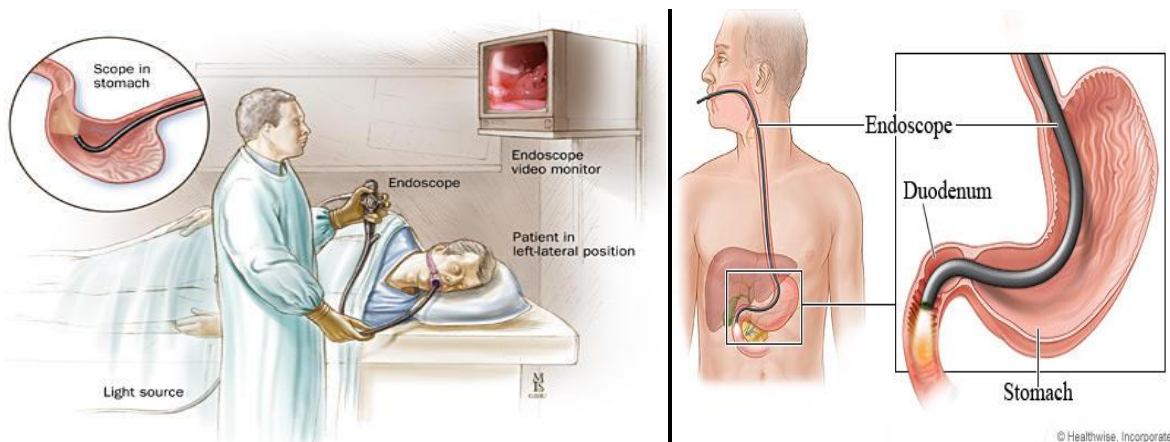
### **3.12 Complications**

Colonoscopy is generally a safe procedure, and complications are rare. Such complications may include the following:

- Colonic perforation
- Bleeding
- Infection
- Abdominal distention
- Postpolypectomy coagulation syndrome
- Splenic rupture
- Small-bowel obstruction
- Medication effects.

### **3.13 Endoscopy**

An endoscopy is a procedure in which the doctor uses specialized instruments to view and operate on the internal organs and vessels of the body. It allows surgeons to view problems within the body without making large incisions. A surgeon inserts an endoscope through a small cut, or an opening in the body such as the mouth. An endoscope is a flexible tube with an attached camera that allows the doctor to see. The doctor can use forceps (tongs) and scissors on the endoscope to operate or remove tissue for biopsy.



**Fig 3.6: Procedure of Endoscopy**

Endoscopic methods to recognize and treat early gastrointestinal malignancies have increased in recent years. This has resulted in more lesions being diagnosed at an early stage and a shift away from invasive surgery towards endoscopic resection. However, it is necessary for the endoscopist to understand the key principles behind advanced endoscopic diagnosis and the new therapeutic options available. It will examine the general principles behind advanced endoscopy and then examine their application in Barrett's neoplasia, gastric cancer and the dysplasia associated lesions or masses associated with ulcerative colitis. It will focus on the best techniques for each of the above pathology (Greenwald DA, 2015).

### **3.13.1 Need for Endoscopy:**

Doctor may order an endoscopy to visually examine an organ. An endoscope's lighted camera allows the doctor to view potential problems without a large incision. A screen in the operating room lets the doctor see exactly what the endoscope sees. The doctor may suspect that an organ or specific area of the body is infected, damaged, or cancerous. In this case, the doctor may order an endoscopic biopsy. An endoscopic biopsy involves using forceps in an endoscope to remove a small sample of tissue. They will send the sample to a lab for testing. The doctor will review the symptoms, perform a physical examination, and possibly order some blood tests prior to an endoscopy. These tests will help the doctor gain a more accurate understanding of the possible cause of the symptoms. These tests may also help them determine if the problems can be treated without an endoscopy or surgery.

### **3.13.2 Types of Endoscopy:**

Endoscopies fall into categories, based on the area of the body that they investigate. The American Cancer Society (ACS) lists the following types of endoscopies:

- Arthroscopy is used to examine joints. The scope is inserted through a small incision near the joint being examined.
- Bronchoscopy is used to examine lungs. The scope is inserted into the nose or mouth.
- Colonoscopy is used to examine the colon. The scope is inserted through the anus.
- Cystoscopy is used to examine the bladder. The scope is inserted through the urethra.
- Enteroscopy is used to examine small intestine. The scope is inserted through mouth or anus.
- Hysteroscopy is used for the examining the inside of uterus. The scope is inserted through vagina.
- Laparoscopy is used to examine abdominal or pelvic area. The scope is inserted through a small incision near the area that's being examined.
- Laryngoscopy is used to examine voice box, or larynx. The scope is inserted through mouth or nostril.
- Mediastinoscopy is used to examine the area between the lungs called the "mediastinum." The scope is inserted through an incision above the breastbone.
- Upper gastrointestinal endoscopy is used to examine the esophagus and upper intestinal tract. The scope is inserted through mouth.
- Ureteroscopy is used to examine the ureter. The scope is inserted through urethra.

### **3.13.3 Risks of an Endoscopy:**

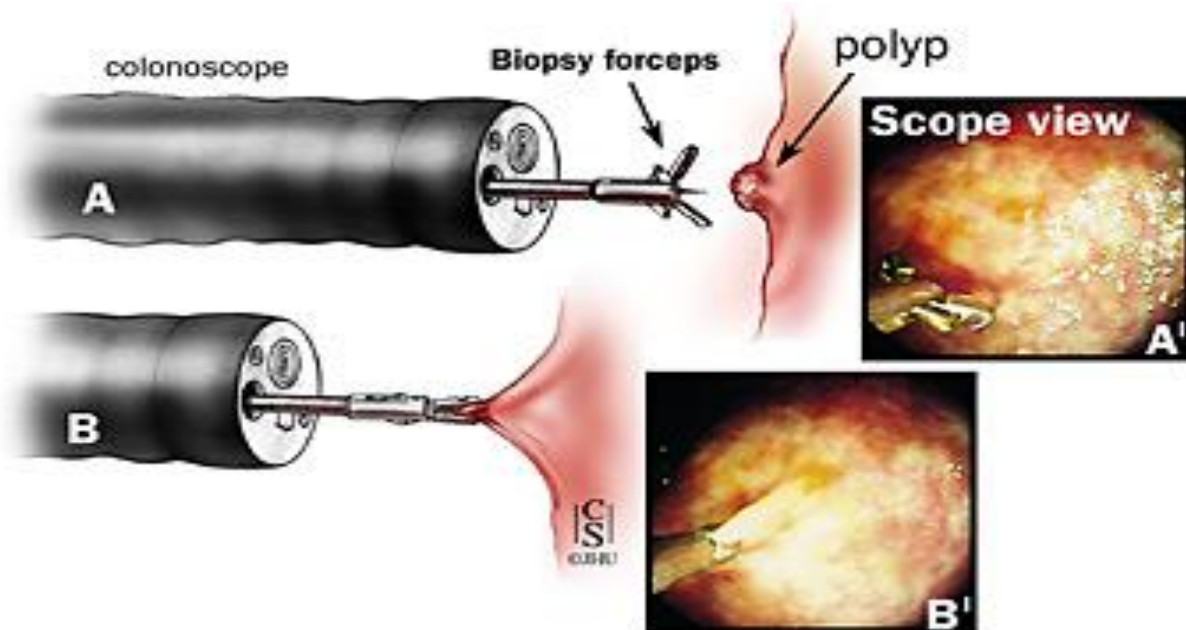
Endoscopy has a much lower risk of bleeding and infection than open surgery. Still, endoscopy is a medical procedure, so it has some risk of bleeding, infection, and other rare complications such as:

- Chest pain
- Damage to organs, including possible perforation
- Fever

- Persistent pain in the area of endoscopy
- Redness and swelling at the incision site

The risks for each type depend on the location of the procedure and own condition. For example, dark-colored stools, vomiting, and difficulty swallowing after a colonoscopy could indicate that something is wrong.

### 3.14 Biopsy



**Fig 3.7: Procedure of Biopsy**

A biopsy is a sample of tissue taken from the body in order to examine it more closely. A doctor should recommend a biopsy when an initial test suggests an area of tissue in the body isn't normal. Doctors may call an area of abnormal tissue a lesion, a tumor, or a mass. These are general words used to emphasize the unknown nature of the tissue. The suspicious area may be noticed during a physical examination or internally on an imaging test. Biopsies are most often done to look for cancer. But biopsies can help identify many other conditions. A biopsy might be

recommended whenever there is an important medical question the biopsy could help answer (Understanding 2015). Examples are given below:

- A mammogram shows a lump or mass, indicating the possibility of breast cancer.
- A mole on the skin has changed shape recently and melanoma is possible.
- A person has chronic hepatitis and it's important to know if cirrhosis is present.

In some cases, a biopsy of normal-appearing tissue may be done. This can help check for cancer spread or rejection of a transplanted organ. In most cases, a biopsy is done to diagnose a problem or to help determine the best therapy option.

### 3.14.1 Types of Biopsies:

- **Needle biopsy.** Most biopsies are needle biopsies, meaning a needle is used to access the suspicious tissue.
- **CT-guided biopsy.** A person rests in a CT-scanner; the scanner's images help doctors determine the exact position of the needle in the targeted tissue.
- **Ultrasound-guided biopsy.** An ultrasound scanner helps a doctor direct the needle into the lesion.
- **Bone biopsy.** A bone biopsy is used to look for cancer of the bones. This may be performed via the CT scan technique or by an orthopedic surgeon.
- **Bone marrow biopsy.** A large needle is used to enter the pelvis bone to collect bone marrow. This detects blood diseases such as leukemia or lymphoma.
- **Liver biopsy.** A needle is injected into the liver through the skin on the belly, capturing liver tissue.
- **Kidney biopsy.** Similar to a liver biopsy, a needle is injected through the skin on the back, into the kidney.
- **Aspiration biopsy.** A needle withdraws material out of a mass. This simple procedure is also called fine-needle aspiration.
- **Prostate biopsy.** Multiple needle biopsies are taken at one time from the prostate gland. To reach the prostate, a probe is inserted into the rectum.

- **Skin biopsy.** A punch biopsy is the main biopsy method. It uses a circular blade to get a cylindrical sample of skin tissue.
- **Surgical biopsy.** Either open or laparoscopic surgery may be necessary to obtain a biopsy of hard-to-reach tissue. Either a piece of tissue or the whole lump of tissue may be removed.

When colonoscopy was performed in our patients, doctor took a tissue for biopsy if it was found abnormal.

# **CHAPTER 04**

## **RESULTS**

## Results

It was found that 3 patients have been diagnosed as colorectal cancer; among 2 were associated with rectal bleeding and 1 was associated with irregular bowel habit.

**Table 4.1: Total number of patient's undergone colonoscopy, endoscopy and biopsy procedure**

Total no of Patients N=100	Colonoscopy	Endoscopy	Biopsy
Under Colonoscopy =26	26	16	4
Male n=19   Female n=7			

Table 4.1 shows Total number of patients' undergone colonoscopy, endoscopy and biopsy procedure. A total number study patient was 100. A total of 19 were male and 7 were female. Among 26 patients undergone colonoscopy, 16 patients were advised to do endoscopy and 4 patients' tissue sample was taken for biopsy procedure.

**Table 4.2: Demography and clinical characteristics of the patients (n=26)**

Clinical characteristics	No of patients Sex: Male-19, female-7
Rectal Bleeding	14
Abdominal Pain	6
Irregular/Change in bowel habit	7
Diarrhea, Dysentery, Constipation, Acidity	9
Hypertension	7
Diabetes Mellitus	6

Table 4.2 shows demography and characteristics of the patients. Among 26 patients, 19 male and 7 female patients were undergone endoscopy and colonoscopy. Fourteen patients had the history of rectal bleeding, 6 patients had abdominal pain and 7 had the history of irregular or change in



bowel habit. Other 9 patients suffered from diarrhea, dysentery, constipation and acidity. Seven patients had medical history of hypertension and 6 had diabetes mellitus.

**Table 4.3: Factors, Main Symptoms &Diagnosis of patients**

No of Cases with patients	Carcinoma	Polyps	Inflammatory Bowel Disease	Hemorrhoid	Diverticular Disease	NAD/AD
Change in bowel habits (7)	No	1	1	1	No	NAD (4)
Blood mixed with stool (1)	1	1	1	No	No	AD
Rectal Bleeding (14)	2	1	4	9	No	AD
Weight loss (2)	No	No	No	No	1	NAD (1)
Diarrhea & Constipation (9)	No	1	No	1	No	AD
Abdominal pain (6)	No	No	2	No	No	NAD (4)

**NAD=No abnormality detected; AD=Abnormality detected**

Table 4.3 shows the factors, main symptoms and diagnosis of the patients. Seven patients had change in bowel habits symptoms, after diagnosis 1 patient had polyps, 1 patient had inflammatory bowel disease, and 1 patient had hemorrhoids. No abnormality has been detected in 4 patients. Another 1 patient had blood mixed with stool symptoms. After diagnosis this patient had detected carcinoma, polyps and inflammatory bowel disease.

A symptom of rectal bleeding patient was found in 14 patients. After diagnosis of these group of patients, 2 patients had carcinoma, 1 patient had polyps, 4 patients had inflammatory bowel disease and 9 patients had hemorrhoids. Two patients had weight loss symptoms, after diagnosis it was found that 1 patient had diverticular disease and another patient had no abnormality.

Nine (9) of the patients had symptoms of Diarrhea and Constipation. After diagnosis it was found that 1 patient had polyps and 1 patient had hemorrhoids. A total of 6 patients had suffered from abdominal pain symptoms. After diagnosis it was found that 2 patients had inflammatory bowel disease and no abnormality has been detected in 4 patients.

**Table 4.4: Final diagnosis of the patients (n=26)**

Endoscopy n=16		Colonoscopy n =26		Detection of Colon cancer N=16	
NAD	AD	NAD	AD	YES	No
9	7	10	16	3	13

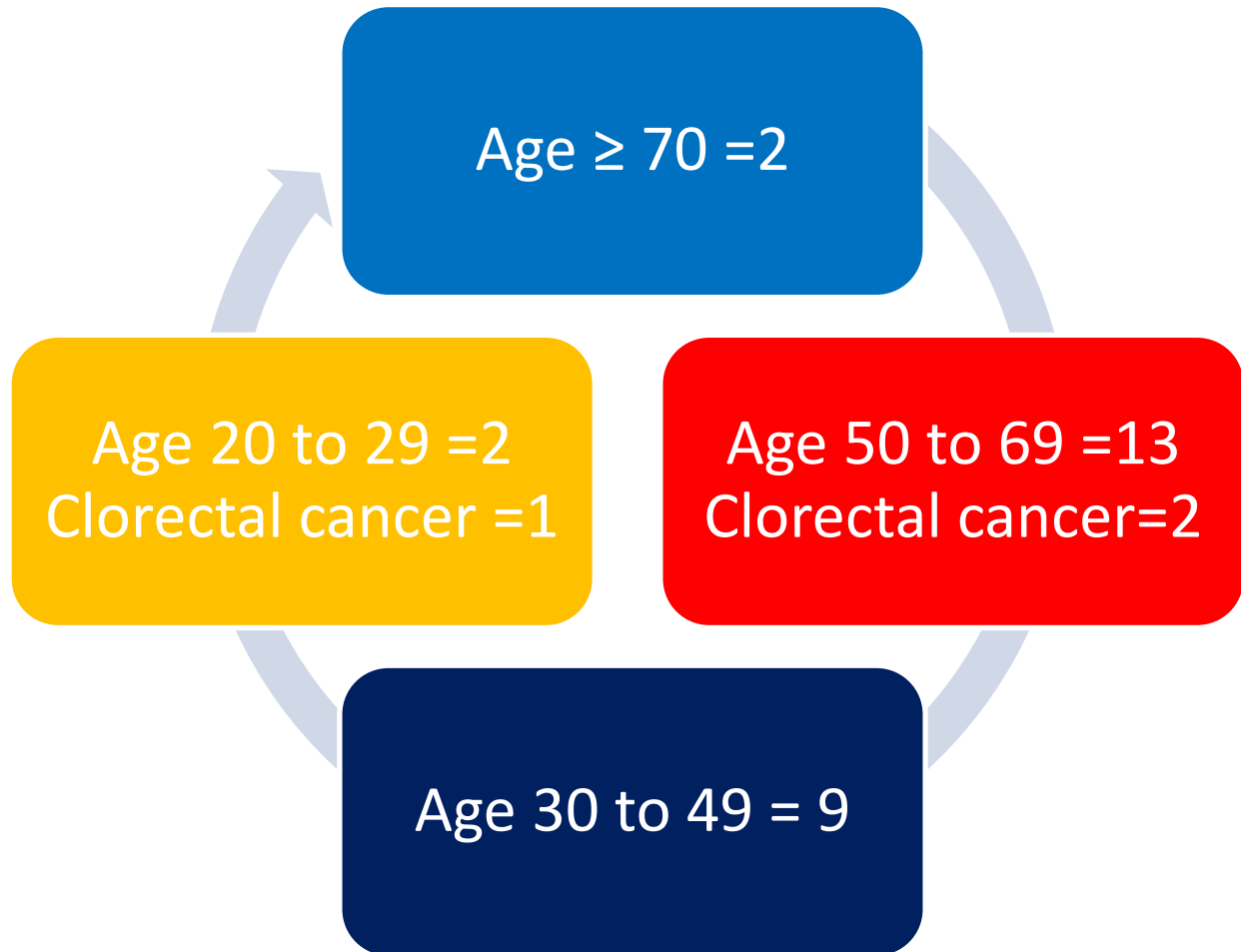
**NAD= No abnormality detected; AD= Abnormality detected**

Table 4.4 shows the final diagnosis of the patients. Twenty six patients had undergone colonoscopy and 16 patients had undergone endoscopy procedure. It has been found from the endoscopy that 9 patients had no abnormality of upper GI symptoms. However, seven patients had some abnormalities where 3 had gastro esophageal reflux disease (GERD), 2 had duodenal ulcer and other 2 had inflammation in the lining tissue of the stomach.

Colonoscopy procedure revealed that 16 patients had different types of disease in the colons. Ten patients had hemorrhoids located in the wall of anus. Four patients had sigmoid colon and 1 had polyps in the ascending colon. Rectal ulcer was found in 1 patient. The histopathology reports revealed that out of 16 patients who had some abnormality in colon, 2 were diagnosed with adenocarcinoma. Both the patients had rectal bleeding and abdominal pain.

One patient had sigmoid colon and another had 0.5 cm polyps in ascending colon. One of the patients came to the hospital that had low anterior resection for rectal cancer. He had history of blood in stool and incomplete bowel motion. Colonoscopy indicated that the patient had no further growth in colon. However, the patient had lymph node metastases.

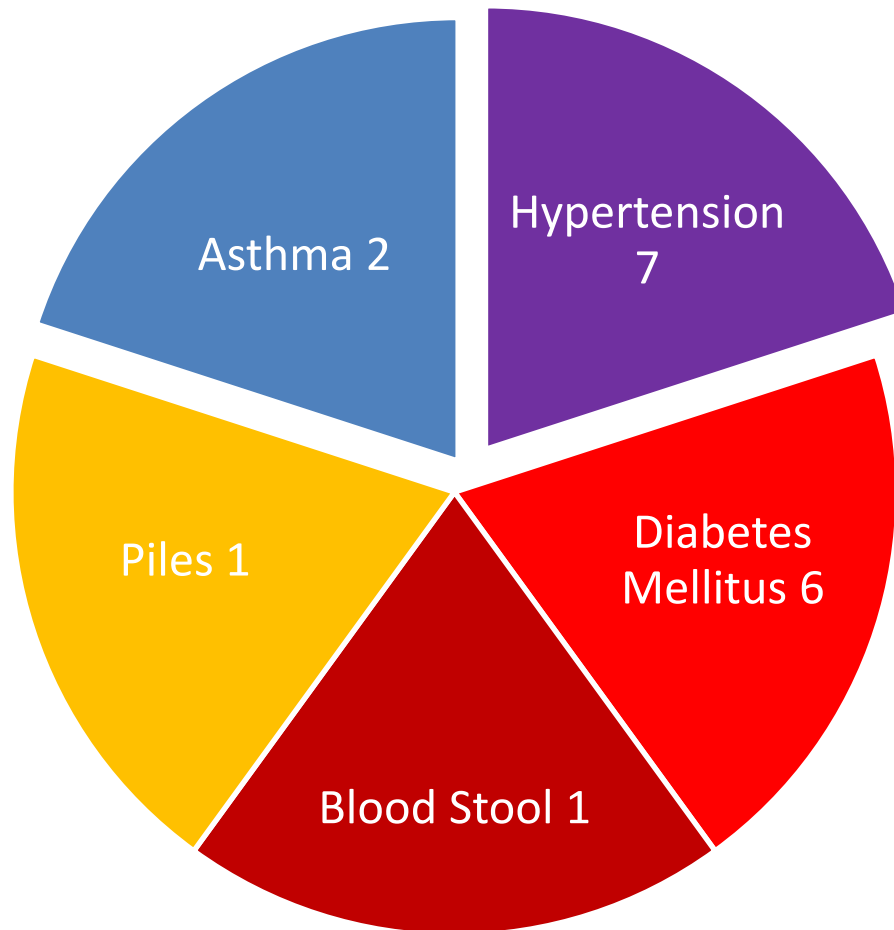
#### 4.1 Age group of Patients undergone Colonoscopy and Endoscopy



**Fig 4.1: Age group of patients undergone Colonoscopy and Endoscopy**

Fig 4.1 shows the age (years) of the patients undergone colonoscopy and endoscopy. Among them the age of the 2 patients was over 70, 13 patients were between 50 and 69. Two patients had colorectal cancer within the age group between 50 and 69. There were 9 patients found from age 30 to 39 years and 2 patients found from age group 20 to 29.

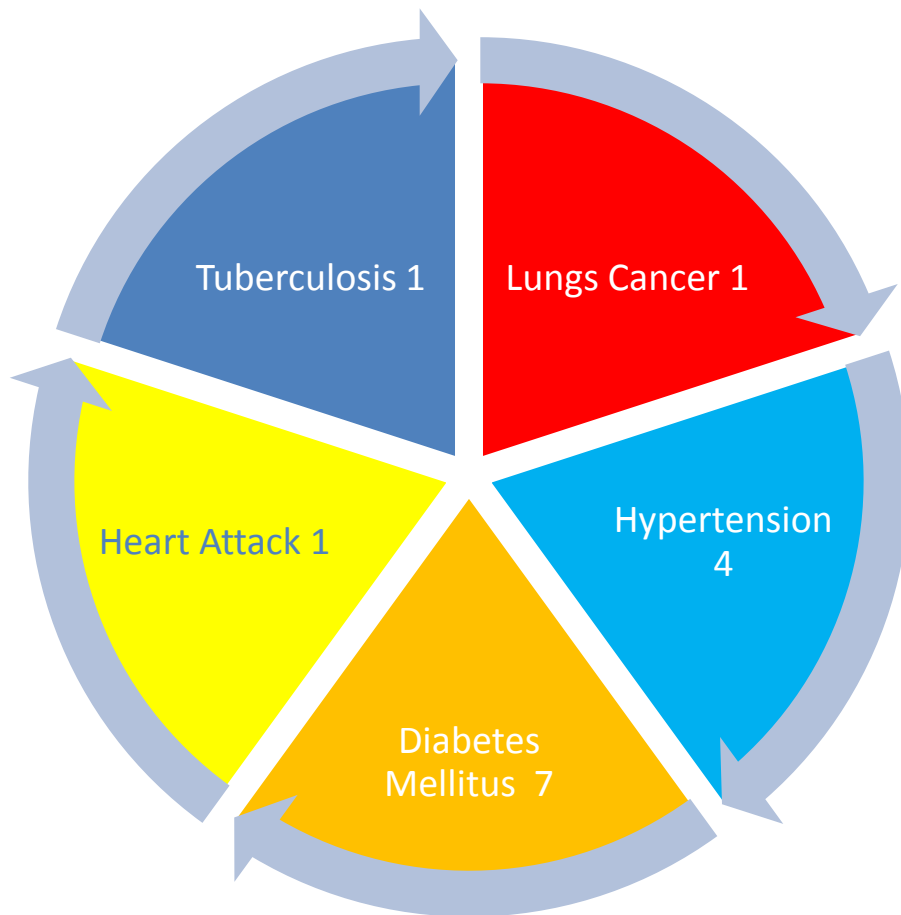
#### 4.2 Past Medical History of the Patients



**Fig4.2: Past Medical History of the patients**

Fig 4.2 shows the past medical history of the patients. It was found that 7 patients had hypertension and 6 patients had diabetes mellitus. It has been from the past medical history that 1 patient had stool of blood, 1 patient suffered from piles and 2 patients had asthma.

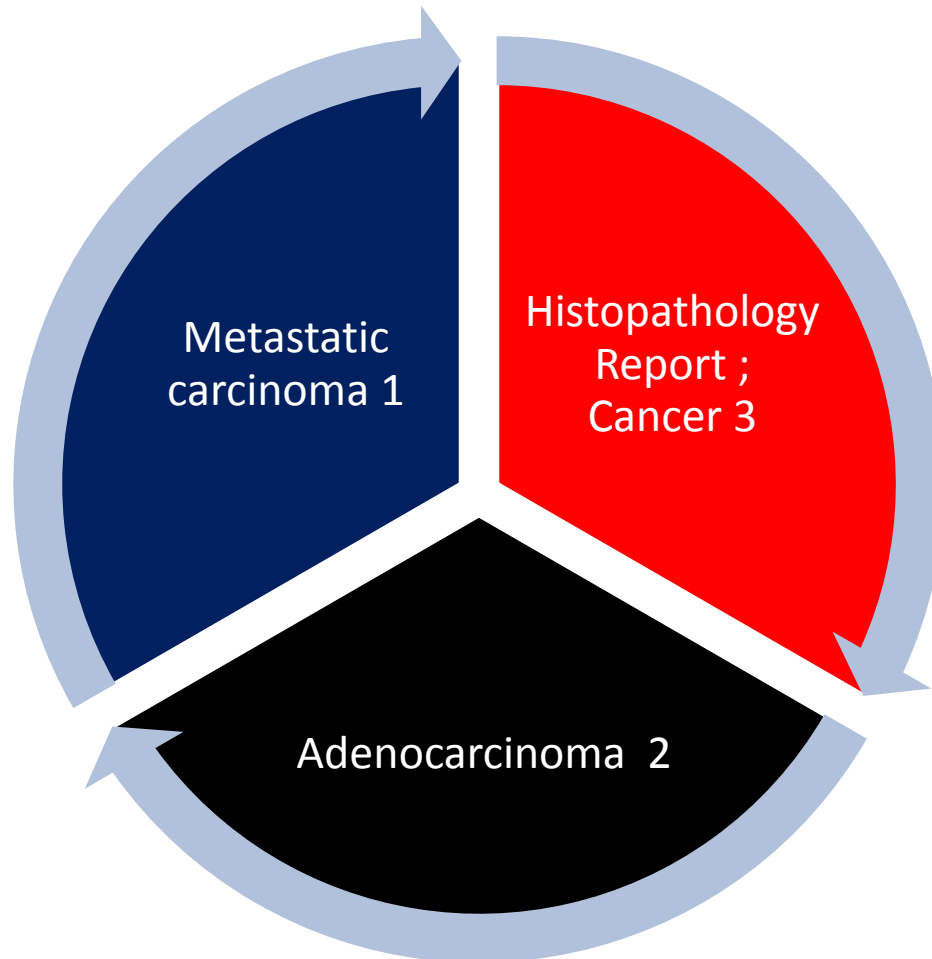
### 4.3 Family History of the Patients



**Fig 4.3: Family History of the Patients**

Fig 4.3 shows that family history of the patients. It was found that one of the patients had the family history of lung cancer. Four 4 patients had the family history of hypertension. Diabetes mellitus was found from the family history of 7 patients. Other family history included heart attack (1 patient) and tuberculosis (1 patient).

#### 4.4 Histopathology Report and number of Cancer Patients



**Fig 4.4: Histopathology Report and number of Cancer Patients**

Fig 4.4 shows that histopathology report and number of cancer patients. It was found that 3 patients had cancer, among 2 patients had adenocarcinoma and 1 patient had metastatic carcinoma.

# **CHAPTER 05**

## **DISCUSSION AND CONCLUSION**

## **Discussion and conclusion**

Colorectal cancer (CRC) is the major public health problems all over the world and rectal bleeding may associated with colorectal cancer. CRC is the third most commonly diagnosed cancer in both men and women. In 2017, there will be an estimate of 95,520 new cases of colon cancer and 39,910 cases of rectal cancer in the United States. While the numbers for colon cancer are fairly equal in men (47,700) and women (47,820), a larger number of men (23,720) than women (16,190) are diagnosed with rectal cancer.

Patients of sex, presenting the rectal bleeding, and visiting to a hospital in Dhaka city were enrolled in our study. Colonoscopy, endoscopy and the biopsy were done to the patients according to the advice by the physician depending on the signs and symptoms of the patients. A total of 100 patients enrolled in this study. Among them 14 patients had the history of rectal bleeding, 6 patients had abdominal pain and 7 had the history of irregular or change in bowel habit. Nine patients suffered from diarrhoea, dysentery, constipation and acidity. Seven and 6 patients had medical history of hypertension and diabetes mellitus respectively. Sixteen patients had undergone endoscopy procedure where 9 patients had no abnormality of upper GI symptoms. However, 3 had gastro esophageal reflux disease (GERD), 2 had duodenal ulcer and other 2 had inflammation in the lining tissue of the stomach. Colonoscopy procedure revealed that 16 patients had different types of disease in the colons. Among 16 patients who had some abnormality in colon, 2 were diagnosed with adenocarcinoma by histopathology result. Both the patients had rectal bleeding and abdominal pain. One patient had lymph node metastases. He had history of low anterior resection for rectal cancer and colonoscopy indicated that the patient had no further growth in colon.

Incidence rates of CRC are highest in Alaska Natives (91 per 100,000) and African Americans (49 per 100,000) and lowest in Asian Americans and Pacific Islanders (32 per 100,000). Reliable statistics on deaths from colon and rectal cancers separately are not available because almost 40% of deaths from rectal cancer are misclassified as colon cancer on death certificates. CRC incidence rates continue to decline in people 50 and older, dropping by 32% just since 2000. This trend is thought to be largely a result of screening, which can prevent CRC by detecting and removing precancerous polyps. Although there is advancement in the screening procedure of



CRC and the use of chemotherapeutic agents, metastasis is developed in approximately 50% of the CRC patients (Kindler H, 2001). According to the American Joint Committee on Cancer staging system, advanced stage is defined as stage III, whereas stage IV is defined as distant metastasis (Corley D, 2014). Colonoscopy is an important tool for diagnosis of colorectal cancer and polyps (Uraoka, T, 2015).

Rectal bleeding may be associated with CRC which is considered as a major symptom of the disease. However, the symptom of bleeding is infrequently reported to the general practitioner (Pedersen AF, 2013). The associated risk factors of CRC include age (over 50 years), consumption of high fat diet, daily alcohol use, sedentary life style, obesity, history of polyps etc. Mortality is very high in patients who diagnosed with CRC at a later stage (Robertson R, 2006). In this study our patients suffered from rectal bleeding. History of polyps has been observed in our patients as well.

It has been reported from a study that one in ten patients with new onset of rectal bleeding had either CRC or colonic adenoma. In this study among 265 patients aged 45 years or above, 15 patients have colorectal cancer, 13 patients were diagnosed with colonic adenoma during 10 year period in a rural general practice in the United Kingdom (du Toit, 2006). Polyps begin in the cells of glandular structures lining the colon. Most polyps are benign; however, Colon Adenomatous Polyp is the cause of greater concern. The growth is associated with DNA changes in the lining of the colon. Up to 10% of these polyps can become cancerous within a 10 year period if undetected or ignored. Another study showed that among 208 patients aged 40 and above with rectal bleeding, 15.4% found to have CRC and 7.7% have polyps. It has been also shown from the same study that 156 patients reported first episode of rectal bleeding or changes in their usual bleeding pattern. Among them 21 patients had CRC (Nørrelund N, 1996). In our study seven patients had change in bowel habits symptoms, after diagnosis 1 patient had polyps, 1 patient had inflammatory bowel disease, and 1 patient had hemorrhoids. Our study has also shown that 1 patient had blood mixed with stool. After diagnosis it was found that this patient had carcinoma, polyps and inflammatory bowel disease.

In our study the symptoms of rectal bleeding was found in 14 patients. After diagnosis of these group of patients, 2 patients had carcinoma, 1 patient had polyps. A study in Belgium showed that among 386 patients with rectal bleeding, 27 had colorectal cancer. Associated sign and

symptoms were recorded as fatigue, weight loss, pain and palpable rectal tumour (Wauters H, 2000). Therefore, our study corroborates the findings of other studies where rectal bleeding has been found to be a risk factor of CRC.

So far to our knowledge no study has been carried out in Bangladesh to find out the incidence of colorectal cancer from patients suffering from rectal bleeding. In Bangladesh perspective this study is very important to know the incidence of the disease along with the age group and sex of patients suffering from CRC.

Vulnerable age group of the Bangladeshi patients diagnosed with colorectal cancer was identified in our present study. The risk factors and symptoms of the patients with CRC was also determined in those patients. Early diagnosis, symptoms indicative of a high risk of cancer will be useful in order to improve survival rate of the patients.

# **CHAPTER 06**

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