INTRODUCTION

Diverticulosis, also known as "**diverticular disease**", is the condition of having diverticulae in the colon, which are outpocketings of the colonic mucosa and submucosa through weaknesses of muscle layers in the colon wall. These are more common in the sigmoid colon, which is a common place for increased pressure [1].

Most people with uncomplicated colonic diverticulosis are asymptomatic[2]. Asymptomatic diverticulosis is a common condition. The incidence of diverticulosis increases with age, from less than 5% before age 40 years to greater than 65% by age 85 years[3].

A small fraction of patients with uncomplicated diverticulosis may have troublesome symptoms, such as colicky abdominal pain, bloating, flatulence, or altered bowel habit. The symptoms characteristically disappear after defecation or passage of flatus. On clinical examination, they may have tenderness in the left iliac fossa with no signs or symptoms of peritonitis or systemic illness, and all laboratory values may be within normal limits. The clinical picture of symptomatic uncomplicated diverticulosis often overlaps with that of irritable bowel syndrome (IBS), because these two clinical entities are usually diagnosed after other pathologies are excluded. IBS-type symptoms are independent of the

presence or absence of diverticulosis on double-contrast barium enema studies.

On the other hand, bleeding alone can sometimes be the only sign of diverticulosis[2].

The diagnosis of symptomatic diverticular disease is one of exclusion in patients with diverticula. Traditionally, diverticula are identified by barium enema, and additional investigations are performed as indicated to rule out other potential causes of symptoms in individual patients. Although computed tomography (CT) has been used commonly in the investigation of diverticular disease, the morphology of diverticular segments makes the diagnosis of underlying cancer difficult even with ideal technique[4].

Infection of a diverticulum can result in diverticulitis. This occurs in 10%-25% of people with diverticulosis. Tears in the colon leading to bleeding or perforations may occur; intestinal obstruction may occur (constipation or diarrhea does not rule this possibility out); and peritonitis, abscess formation, retroperitoneal fibrosis, sepsis, and fistula formation are also possible occurrences. Rarely, an enterolith may form. Diverticular disease was found associated with a higher risk of left sided colon cancer [5].

No treatment or follow-up needs to be offered to patients who are asymptomatic, although there may be a prophylactic

benefit of a high-fibre diet. The risk of perforation may be increased by the use of NSAIDs and long-term use of opioids[6].

According to available guidelines, treatment of symptomatic, but uncomplicated, diverticular disease aims to reduce the frequency and severity of diverticular-related symptoms (abdominal pain, bloating, alterations in bowel habit) and to prevent complications. Different agents have been proposed, such as bulking agents, antispasmodics, and topical antibiotics, on the basis of different potential pathophysiological mechanisms; that is, abnormal colonic motility, inadequate intake of dietary fibers, intestinal bacterial overgrowth, and mucosal inflammation[7].

Most patients admitted with acute diverticulitis will respond to conservative treatment, but 15-30% will need surgery. The indications for surgery are purulent or faecal peritonitis, uncontrolled sepsis, fistula, obstruction, inability to exclude carcinoma[6].

For emergency surgery, a recent multicentre randomised controlled trial found that a one-stage procedure (primary anastomosis) significantly reduced rates of postoperative peritonitis and emergency re-operation compared with a two-stage procedure (formation of an end colostomy with oversewing of the rectal stump - Hartmann's procedure)[6].

Aim Of The Work

The aim of this study is to review the recent available tools in the diagnosis and management of patients with diverticular disease especially cases with complications which may be difficult to manage challenging the expert surgeons.

Chapter 1

PATHOPHYSIOLOGY OF DIVERTICULAR DISEASE

Diverticular disease of the colon is the most frequent anatomical colonic alteration, which is detected frequently during colonoscopy[8].

Colonic diverticular disease is a major health problem among middle-aged and especially old people in the Western world [9] and its clinical management is challenging and currently changing [10]. This is due to variations of its clinical presentation forms and pathophysiology. In contrast to the relatively limited scientific efforts presented in this field, diverticular disease is of high frequency in relation to for example inflammatory bowel disease, which is less frequent and even less life threatening [11]. For these reasons, diverticular disease has been named as the "neglected disorder" [12]. Current data demonstrate its mortality rate as 2.5 per 100,000 persons per year [9].

Definition

Diverticular disease is an alteration of the colonic wall structure characterized by the presence of pockets called 'diverticula'. These diverticula are characterized by herniation of the colonic mucosa and sub-mucosa through defects in the

muscle layer at the weakest points in the colonic wall where blood vessels penetrate the wall of colon[13].

Diverticulae are covered by serosa only, and develop at four well-defined points around the circumference of the colon, where the vasa recta penetrate the muscular layer (Fig. 1) [14].

Diverticulae vary from solitary findings to many hundreds. They are typically 5-10 mm in diameter but can exceed 2 cm (Figs. 2, 3) [15].

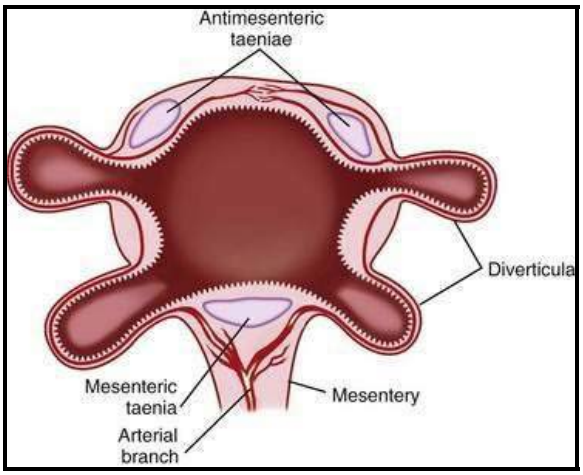

Fig. (1): Showing colonic diverticula and their relationship to the taenia coli [14].

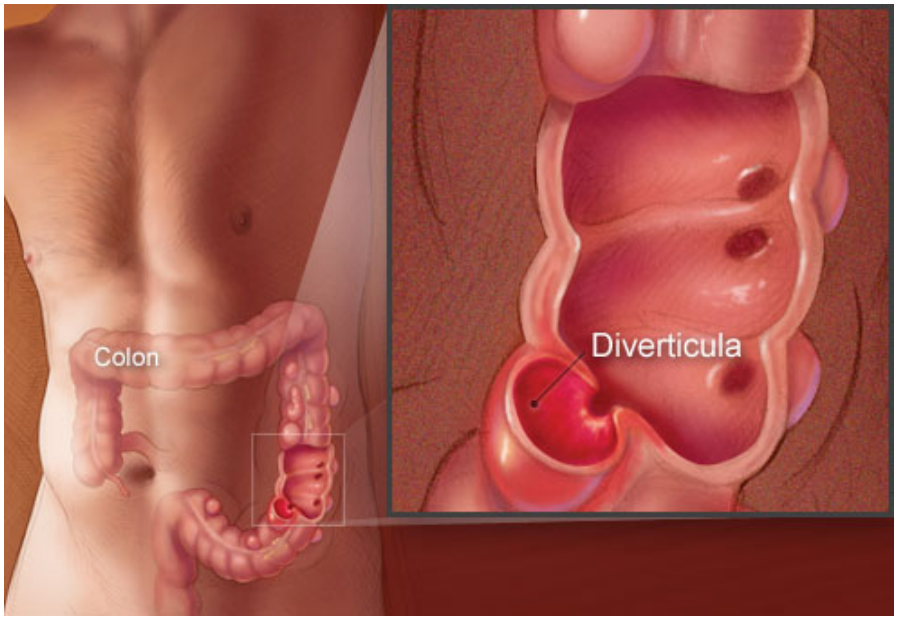

Fig. (2): Showing sigmoid colon with diverticulosis [15].

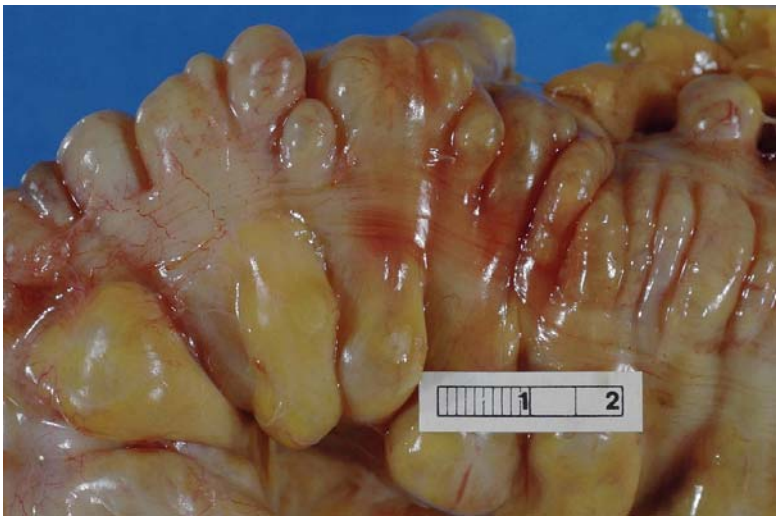

Fig. (3): Large bowel (sigmoid colon) showing multiple diverticula. The diverticula appear on either side of the longitudinal muscle bundle (taenium)[15].

Types of Diverticula

Diverticula occur commonly in the sigmoid and descending colon which is a common place for increased pressure. However it can occur at any site throughout the gastrointestinal tract. As herniation here is not through all colonic layers, these are called **pseudo diverticula** [16].

While diverticulosis occurring in the right colon is characterized by herniation of all colonic wall layers, which are actually **true diverticula** [13].

Right-sided diverticulosis is more common in Asian people. Recently, Yamada *et al*. found that right-sided colonic diverticulosis (True Diverticulae) is 21.6% in comparison with left-sided or bilateral diverticulosis (Pseudodivertculae) which was 18.6% of Japanese people undergoing colonoscopy[17].

Epidimiology

By the age of 50 years old, approximately 50% of all people have diverticula, and nearly 70% of all people have diverticula by the age of 80 years old [18].

Diverticular disease is rare in people younger than 40 years. But is more virulent, with a high risk of recurrences and complications[19].

Diverticular disease has no sex predominance, as males and females are equally affected[7].

Most people with colonic diverticulosis remain asymptomatic, however about 20% of these patients will develop symptoms, which is called 'diverticular disease' (DD)[8]. 15 % of whom will ultimately develop complications. DD has a significant burden on westernized National Health Systems[20] (Fig. 4).

For many years, it had been thought that diverticulosis exclusively affect the westernized world due to lack of diet fibre and increased pressure at the colonic wall[21]. However, recent data have revealed an increase in the prevalence of colonic diverticulosis throughout the world[22].

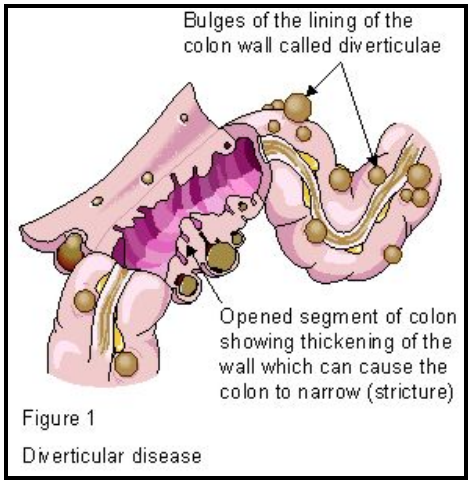

Fig. (4): Drawing showing a sigmoid colon with many diverticula[23].

Pathophysiology

The underlying pathological mechanisms cause the formation of colonic diverticula, These are likely to be the result of complex interactions among diet, colonic microbiota, genetic factors, colonic motility, microscopic inflammation and structure. All these factors have to be considered as potential targets of treatment[24].

Pathogenesis of diverticulosis

1- Dietary aspects

Role of the Western "Low-Fibre Diet"

Burkitt and Painter suggested the pathogenetic role of a low-fiber diet in 1970s. Diverticulosis is of high prevalence in Western world due to lack of fibre in diet, in contrast with rural Africa where diverticulosis is of low frequency due to high fibre diet. Individuals moving from rural areas to urban environments develop diverticulosis more frequently [25].

However, recent investigations have decreased the relationship between low-fiber diet and diverticulosis [26]. The association between low-fiber diet and diverticulosis does not seem to have a role in the initiation of DD complications, i.e., diverticulitis and diverticular bleeding.

In the "Health Professionals Follow-up Study" 47,228 males were followed for 18 years, 801 participants experienced diverticulitis and 383 diverticular bleeding. The study showed

that there is no difference in DD incidence regarding consumption of nut, corn, or popcorn on multivariate analysis[27]. The same study revealed an increased incidence of diverticulitis and diverticular bleeding in obese patients [28] and among patients with decreased physical activity[29]. Furthermore, diverticular bleeding and also diverticulitis were increased among users of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) [30].

Other dietary factors

Vegetable in diet and especially a "strict vegetable diet" have been shown to decrease the incidence of diverticular disease. By contrast, consumption of alcohol, coffee or caffeine do not have a pathogenetic role in diverticular disease [31].

2- Imbalance of colonic microflora

An imbalance of the colonic microflora also has a pathogenetic factor in diverticular disease of the colon [32]. Colonic microflora has been affected after the "dietary shift" which has been observed through the past century. Decreased fiber in diet leads to increased levels of bacteroides and decreased levels of bifidobacteria[31].

Intestinal microbiome composition have been found for a number of intestinal disorders and their Disease-specific variations. Preliminary information on colonic microbiota alteration is also becoming available. Using a polymerase chain reaction-based profiling technique on DNA isolates from faecal

samples, Daniels *et al*. recently compared the faecal microbiota of diverticulitis patients with control subjects from a general gastroenterological practice. They found that Firmicutes/ Bacteroidetes ratios and Proteobacteria load were comparable among patients and controls ($P = 0.20$), while a higher diversity in diverticulitis for Proteobacteria ($P < 0.00002$) [33].

3- Structural changes of the colonic wall

A- Changes of the connective tissue fibers

There are many lines of evidence to suggest that different alterations of the connective tissue predispose individuals for development of colonic diverticula. Diverticulosis is frequent in patients with connective tissue disorders like Ehlers-Danlos Syndrome, Williams Syndrome or Coffin-Lowry syndrome (Fig. 5) [34].

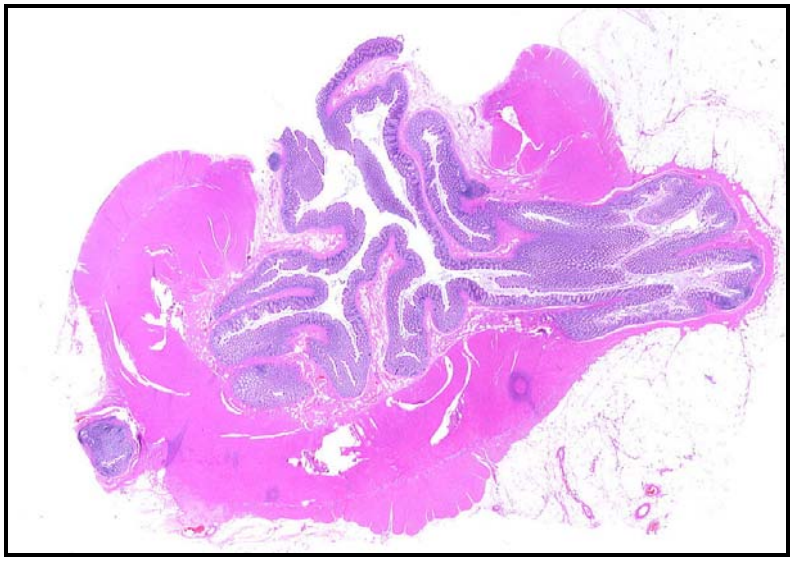

Fig. (5): Shows Whole slide of a transverse section of left colon with diverticulosis[34].

Diverticulosis is also a common finding in *polycystic* kidney disease [35].

Several studies have demonstrated alterations of the connective tissue fibers. An increased cross-linking of collagen has been described, as well as increased levels of collagen type III [36] and increased levels of elastin [37].

B- Changes of the musculature

Thickening of the muscular layers has been described as one of the most consistent features of colonic diverticulosis [38].

The thickening of longitudinal and circular muscles in diverticular disease is neither hyperplastic nor hypertropic, but appears to be related to the contractile state. An increase in the number of elastic fibers has been observed only in the longitudinal muscle. It has been suggested that this process is responsible for longitudinal contraction, with subsequent thickening of both muscle layers. All these changes, along with elastin deposition in the teniae coli, lead to an irreversible state of contracture, with substantial bowel shortening, which may result in decreased resistance of the colon wall to persistent intraluminal pressure[39].

C- Enteric neuropathy

Several studies have suggested a concept of diverticulosis as an enteric neuropathy. A derangement of the

myenteric nerve plexus in diverticulosis has first been suggested [40].

A decreased number of Cajal cells and glial cells within the myenteric plexus—regarded as the "pacemaker of colonic motility"—have been described in contrast to normally represented enteric neurones [41]. A recently published morphologic and morphometric study showed myenteric and submucosal oligoneuronal hypoganglionosis, which was also suggested as morphologic correlative for apparent functional intestinal motor abnormalities[40].

4- Functional abnormalities of the colon

A- Colonic motility and increased intracolonic pressures

The concept regarding the role of colonic motility for diverticula formation does also go back to Painter who was the first to report results from manometric and myoelectric in vivo studies [42].

These investigations have shown that patients with diverticular disease exhibit dysmotility with increased intracolonic pressures, more frequent high-amplitude propagated contractions and "tonic segmenting". Chronic excessive segmental contractions which lead to a "concertina-like colonic wall (bladder colon)" have been suggested as the origin of symptoms, painful sensations and eventually functional obstruction [41].

An increased intraluminal colonic pressure has also been suggested as a major pathogenetic factor of diverticula formation . However, not all studies have supported this view and some have suggested, that these increased pressures are only detectable when symptoms occur [43].

The colonic wall has been shown to have deceased elasticity which is due to the altered musculature and connective tissue fibers [44].

Neural degeneration with age may also contribute, with several studies suggesting reduction in neurones in the myenteric plexus[40] and decreased myenteric glial cells and interstitial cells of Cajal[45].

Denervation hypersensitivity has also been reported, and these abnormalities of enteric nerves might lead to uncoordinated contractions and high pressure, producing diverticulosis[46].

The associated muscular hypertrophy and altered enteric nerves[74] may result from remodelling after acute inflammation, which numerous animal studies have shown to be associated with muscular hypertrophy, abnormal motility[48], visceral hypersensitivity and altered neurochemical coding[49].