EVALUATION OF PLATELET INDICES AND RED CELL DISTRIBUTION WIDTH AS EMERGING-BIOMARKER FOR THE DIAGNOSIS OF ACUTE APPENDICITIS AND APPENDICULAR PERFORATION

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LIST OF ABBREVATIONS USED

AA	Acute appendicitis
PA	Perforated appendicitis
CBC	Complete blood count
WBC	White blood cell
RDW	Red blood cell Distribution Width
MK	Megakaryocytes
MPV	Mean Platelet Volume
PDW	Platelet Distribution Width
P-LCR	Platelet Large Cell Ratio
RIF	Right Iliac Fossa
TLC	Total Leucocyte Count
USG	Ultrasonography
CT	Computed tomography
PLT	Platelet count
fL	Femtolitre
EDTA	Ethylenediaminetetraacetic acid

ABSTRACT

TITLE: Evaluation of Platelet indices and Red Cell distribution width as emerging biomarkers for the diagnosis of acute appendicitis and appendicular perforation

Introduction:

Acute appendicitis is a common surgical condition encountered, worldwide. If not treated on time this may result in a life-threatening complication. This study aims to investigate the change in platelet indices like mean platelet volume (MPV) and platelet distribution width (PDW), red cell distribution width (RDW) in relation to the diagnosis of acute appendicitis and its role in the prediction of appendicular perforation.

Methods:

A prospective observational study of 190 patients, who were diagnosed with appendicitis and underwent an appendectomy in our institute was undertaken, which was confirmed histopathologically. Preoperatively blood samples of White blood cells (WBC), platelet count, MPV, PDW and RDW were analysed using a

Sysmex XN1000 analyser machine.

Results:

Of 190 patients,169 patients had acute appendicitis and 21 patients had perforated appendicitis. The mean age of patients was 28.04±14.2. The male to female ratio was 1.5:1. The WBC (p<0.05), MPV (p<0.05) and PDW (p<0.05) were found to have higher statistically significant values in acute appendicitis and perforated appendicitis compared to the RDW (p>0.05). However, perforated appendicitis had a higher RDW value compared to acute appendicitis, which can be a predictive factor.

Conclusion:

The elevated value of MPV and PDW in association with leucocytosis can be used as supportive evidence for the clinical and radiological diagnosis of acute appendicitis and appendicular perforation. Thus, the value of these can be used as diagnostic cost-effective inflammatory biomarkers.

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INTRODUCTION

One of the most typical causes of an acute abdomen is acute appendicitis, occurs almost every day in the surgical department. Despite being aware of the typical signs and symptoms of acute appendicitis, early diagnosis can occasionally be challenging and inconclusive.

In order to prevent complications like perforation and subsequent peritonitis, the option of whether to operate or wait it out in patients with appendicitis remains a conundrum until the diagnosis is certain. A normal appendix may be removed leading to unnecessary risk of morbidity and social burden due to improper symptom interpretation and early surgery [1]. Consequently, a prompt and precise diagnosis is essential.

Surgeons regularly use the complete blood count (CBC), one of the most common requested tests in clinical laboratories, in the emergency room as part of normal preoperative evaluation and to identify inflammatory diseases. The white blood cell (WBC) count and neutrophil count are the early markers of inflammation in acute appendicitis [2]. However, depending on the population being investigated, the severity of the symptoms, and the cut-off values being employed, their sensitivity and specificity can vary greatly [3,4].

Red blood cell size variability is quantified by the red cell distribution width (RDW). RDW has been linked to the identification of a variety of inflammatory diseases, including acute appendicitis, according to studies. The erythrocyte index, a biological marker of inflammation that has been utilised in haematological practise, is currently accepted [5]. Elevated erythrocyte sedimentation rate and interleukin-6 levels are related to high RDW[5,6].

The involvement of platelets in inflammation is critical. The function of platelets in the aetiology of numerous disorders when inflammation occurs has been demonstrated in numerous

studies. The activation of the coagulation system, severe infection, trauma, systemic inflammatory reaction syndrome, and thrombotic disorders have all been linked to variations in platelet indices in these investigations[7].

Platelet indices, including mean platelet volume (MPV) and platelet distribution width (PDW), are indicators of platelet activation and connected to platelet morphology.

The MPV is the average size of the platelet in peripheral blood. The PDW represents variability in platelet size (anisocytosis) and heterogeneity in platelet morphology. An increase in PDW is caused by a change of platelet shape from discoid to spherical with pseudopod formation, which occurs during platelet activation[8].

Appendicectomy is the most common procedure done in a surgical emergency; differential diagnosis of acute appendicitis is still a matter of concern in some atypical cases where delayed or inaccurate diagnosis may lead to several complications. Radiological imaging that helps in surgery decision may not confirm the diagnosis or may not be available in some hospitals.

Hence, we intend to study using basic, inexpensive, readily available, and convenient inflammatory markers presented in CBC to evaluate their value in establishing the diagnosis of acute appendicitis and its role in predicting appendicular perforation.

AIM OF THE STUDY

- To study the relationship between platelet indices (PDW and MPV) and RDW and acute appendicitis and to evaluate its credibility as a new diagnostic marker for acute appendicitis.

- To evaluate whether the change in levels of platelet indices (PDW and MPV) and RDW have a predictive potential for the diagnosis of appendicular perforation.

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE:

The first descriptions of the appendix were dated back to the sixteenth century [9,10]. Although it was first sketched in the notebooks of Leonardo da Vinci around 1500, the appendix was not officially described until 1524 by da Capri[11] and 1543 by Vesalius[12]. In 1554, the French physician Jean Fernel (1497-1558) reported the first case of perforative appendicitis at autopsy[13].

Lorenz Heister (1683–1758), a surgeon and professor of medicine at the German universities of Altdorf–Nürnberg and Helmstedt, is responsible for the first post-mortem description (1712). First to examine the pathology of appendicitis was Heister 1711[14].

The idea of "perityphilitis," which is cecal inflammation, served as the foundation for the pathological theory from the 19th century (blind). The advanced stages of inflammation that were seen in corpses easily explain why the cecum was thought to be the disease's location rather than the appendix.

The first appendicectomy was performed in 1736 by Claudius Amyand, a surgeon at St. George's Hospital in London. The inflamed appendix was perforated with a pin, and the surrounding omentum was excised through a scrotal wound in a chronic inguinal hernia. The Patient was a young 11-year-old boy who recovered well[15]. The first published account of appendicectomy for appendicitis was by Krönlein in 1886.

However, the Patient died two days postoperatively. Fergus, in Canada, performed the first elective appendicectomy in 1883[16]. Charles McBurney (1845-1913) was one of the surgeons working on the diagnostics and operative treatment of appendicitis. McBurney's early operative interference of appendicitis was presented to the New York Surgical Society in 1889. In which he described the area of greatest abdominal pain in this disease process, now known as McBurney's point. Five years later in 1894, he proposed the incision that he used in cases of appendicitis, now

called McBurney's incision. However, McBurney later credited McArthur, who first described this incision[17].

The US surgeon John Benjamin Murphy introduced and popularized early removal of the appendix in all cases of suspected appendicitis. In 1904 he described the triad of pain in the abdomen, vomiting and fever, which remains a sound basis for diagnosis even today[18].

Dawbarn insisted on the use of a purse string suture placed around the base of the appendix. In 1889, Senn first drew attention to the risks of ligature slipping off the appendix stump with subsequent peritoneal contamination. On 13 September 1983, the gynaecologist Professor Kurt Semm performed the world's first laparoscopic appendicectomy at the University of Kielin, Germany[19].

EMBRYOLOGY

Appendix developement is seen during the descent of the colon as a narrow diverticulum from the distal end of the caecal bud, which appears at about 6th week as a small conical dilation of the caudal limb of the midgut[20]. At an early embryonic stage, it has the same caliber as the caecum and is in line with it. It is formed by excessive growth of the right wall of the caecum, which pushes the appendix to the inner side[21].

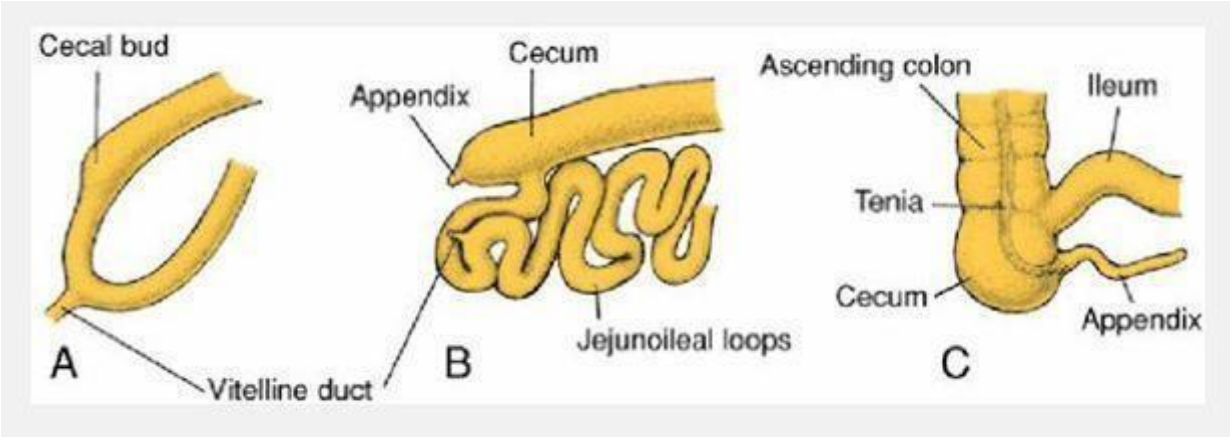


FIGURE 1: Development of appendix

ANATOMY

"The appendix averages 9 cm in length[22], with its outside diameter ranging from 3–8 mm. The base of the appendix is traced by following the teniae coli of the ascending colon to their confluence point at the base of the cecum. The appendiceal tip, however, can vary significantly in location. Frederick first described the various positions of the appendix, comparing the position with the face of an analogy clock33.

11 O clock (0.2%)- Para colic (lies in the sulcus on the lateral aspect of the caecum).

12 O clock (65.28%)- Retrocaecal (lies behind the caecum and may be totally or partially retroperitoneal)

1 O clock (1%)- Pre-ileal

2 O clock (0.2%)- Post ileal

3 O clock (0.05%)- Promonteric (the tip of the organ points towards the sacral promontary).

4 O clock (31.01%)- Pelvic (Appendix dips into the pelvis).

6 O clock (2.26%)- Subcaecal or midinguinal or mid Poupart"

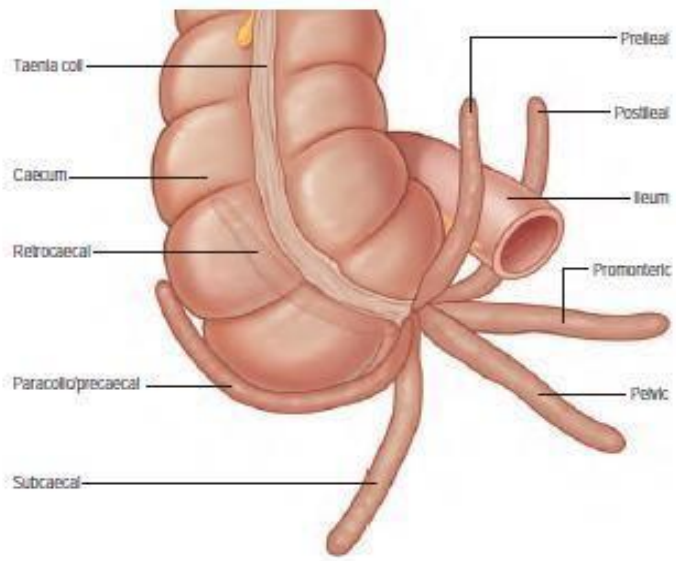


FIGURE 2: Appendicular different position

MESOAPPENDIX

"The mesentery enclosing the appendix is a triangular fold of peritoneum around the appendix. It extends from the lower end of the mesentery of the small intestine close to the ileocecal junction. It encloses the tip of the appendix but sometimes fails to reach the distal third, which leads to a vestigial low peritoneal ridge containing fat present at the distal third. It contains the blood vessels, nerves and lymph vessels of the appendix and usually contains a lymph node".23

The appendix's longitudinal muscle is formed by the convergence of the three taeniae coils that coil on the ascending colon and caecum. It is easier to locate the anterior caecal taenia in clinical practise since it is typically distinct and may be linked to the appendix.

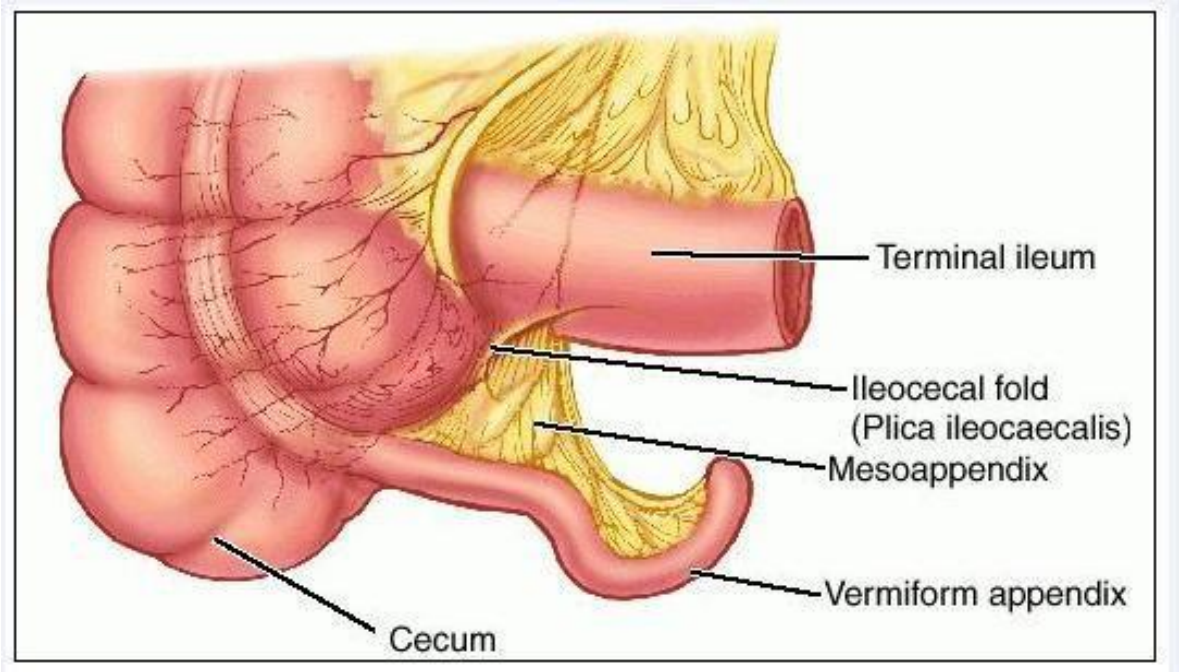


FIGURE 3: Mesoappendix

APPENDICULAR ARTERY:

The main appendicular artery, a branch of the ileocolic artery, enters the mesoappendix near the base of the appendix and runs behind the terminal ileum.

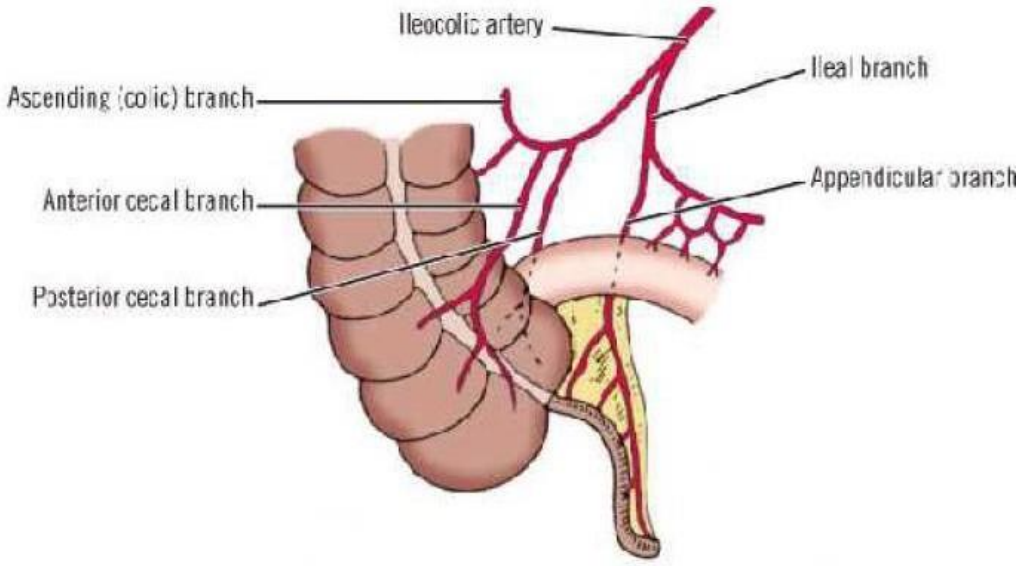


FIGURE 4: Appendix blood supply

APPENDICULAR VEINS:

The appendix is drained by one or more appendicular veins into the ileocolic vein which drains into the superior mesenteric vein.

LYMPHATICS:

Lymphatic vessels in the appendix are numerous: there is abundant lymphoid tissue in its walls. From the body and apex of appendix 8-15, vessels ascend in the mesoappendix and are occasionally interrupted by one or more nodes. They unite to form three or four larger inferior and superior nodes of the ileocolic chain.

INNERVATIONS:

The appendix and overlying visceral peritoneum are innervated by sympathetic and parasympathetic nerves from the superior mesenteric plexus.

HISTOLOGY

MUCOSA

The mucosa is covered by columnar epithelium, and M cells are present in the epithelium that overlies the mucosal lymphoid tissue. Glands (crypts) are fewer in number and thus less densely packed. They penetrate deep into the lymphoid tissue of the mucosal lamina propria.

SUB-MUCOSA

"The submucosa typically contains many large lymphoid aggregates that extend from the mucosa and obscures the muscularis mucosae layer: consequently, this becomes discontinuous. These aggregates also cause the mucosa to bulge into the lumen of the appendix so that it narrows irregularly. They are absent at birth but accumulate over the first ten years of life to become a prominent feature. The submucosal lymphoid tissue frequently exhibits germinal centres within

its follicles, indicative of B-cell activation, as it is in secondary lymphoid tissue elsewhere. In adults, the normal layered structure of the appendix is lost, and the lymphoid follicles atrophy and are replaced by collagenous tissue. In the elderly, the appendix may be filled with fibrous scar tissue".

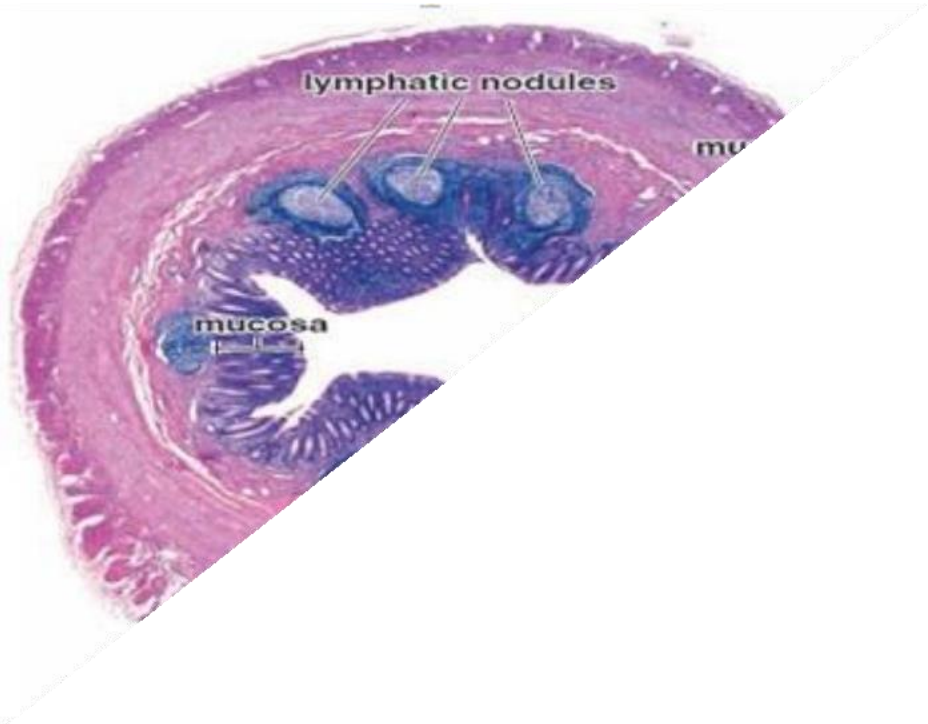


FIGURE 5: Histology of appendix

MUSCULARIS EXTERNA

Outer longitudinal and inner circular smooth muscle layers can be found in the muscularis externa. With the exception of the continuous outer muscle layer covering the majority of the appendix, the longitudinal fibres are arranged in a continuous layer, however under the microscope they appear as longitudinal bands called taeniae coli.

The longitudinal muscle increases near the base of the appendix, forming rudimentary taeniae that are connected with those of the caecum and colon. The longitudinal layer between the taeniae coli is significantly thinner, with a thickness that is less than half that of the circular layer.

SEROSA

The serosa forms a complete covering, except along the mesenteric attachment. The longitudinal muscular fibres form a whole layer of uniform thickness, except over a few small areas where both muscular layers are deficient, leaving the serosa and submucosa in contact.

ACUTE APPENDICITIS

INCIDENCE:

For men, the lifetime appendectomies rate is 12%, and for women, it is 25%. The majority of people who develop appendicitis do so during the second and fourth decades of life, with a mean age of 31.3 years and a median age of 22 years. (M:F 1.2 to 1.3:1)[24] There is a slight male predominance.

ETIOPATHOGENESIS:

A fecolith and, less frequently, a gallstone, tumour, or ball of worms (oxyuriasis vermicularis) are the most common obstructions associated with appendicular inflammation. As mucinous fluid continues to be secreted, intraluminal pressure may eventually build up to the point where draining veins collapse. Furthermore compromising the blood supply, obstruction and ischemia injury then stimulate bacterial development with further inflammatory edema and exudation. In the first stages, subserosal arteries are congested, there is frequently a minor perivascular neutrophilic infiltrate, and there is only a sparse neutrophilic exudate across the

mucosa, submucosa, and muscle is propria. The normally gleaming serosa is replaced by a drab, grainy, red membrane as a result of the inflammatory response. This change suggests early-onset acute appendicitis. Later on, the serosa has a purulent reaction brought on by significant neutrophilic exudates. As the inflammation worsens, an abscess forms inside the wall, along with mucosal ulcerations and necrosis foci. Acute suppurative appendicitis is what this condition entails. As the appendix continues to compress, significant portions of the mucosa develop hemorrhagic green ulcers, resulting in acute gangrenous appendicitis. This is swiftly followed by rupture and suppurative peritonitis. The histological criteria for the diagnosis of acute appendicitis are neutrophilic infiltration in the muscularis, also presence of neutrophils and ulcerations within the mucosa layer[25].

PERFORATED APPENDICITIS:

"When acute appendicitis has progressed to appendiceal perforation, other symptoms may be present. Patients will often complain of two or more days of abdominal pain, but their duration of symptoms may be shorter, as previously discussed. If the surrounding intra-abdominal structures, such as the omentum, have walled off the perforation, the pain is localised to the right lower quadrant; but, if generalised peritonitis develops, the discomfort may become diffuse. The aggravating pain may be so severe that patients do not remember the antecedent colicky pain. Patients with perforation often have rigors and high fevers to 102°F (38.9°C) or above. A history of poor oral intake and dehydration may also be present."

BACTERIOLOGY

The commonly seen organisms in the healthy appendix, in acute appendicitis, and in perforated appendicitis are Escherichia coli and Bacteroides fragilis[25 -27]. Appendicitis is a polymicrobial infection, with some showing the culture report of up to 14 different organisms in patients with perforation.[25]

Aerobic and Facultative	Anaerobic
Gram-negative bacilli	Gram-negative bacilli
Escherichia coli	*Bacteroides fragilis*
Pseudomonas aeruginosa	Other *B-*
Klebsiella species	
Gram-positive cocci	
Streptococcus anginosus	
Other *Streptoc*	
Enter	

TABLE 1: Bacterial infections seen in acute appendicitis

CLINICAL FEATURES:

The classic history is of the gradual onset of central colicky abdominal pain over 24 hours associated with anorexia, nausea, occasionally vomiting (Murphy) and usually constipation. The pain may change when the parietal peritoneum becomes involved in the inflammation, localizing to the right iliac fossa. Pain is aggravated by moving or coughing. Unfortunately, only half the patients give this typical history. In a third of cases, the pain presents over 1-2 days, and it may present in the right iliac fossa. Vomiting may be absent, and diarrhea occurs in 20% of patients. An atypical presentation is common in the very young, elderly and also during pregnancy[28].

ON EXAMINATION:

The Patient looks unwell, may have a facial flush and usually has mild pyrexia. There is often halitosis and slight tachycardia. On examination of the abdomen, signs of generalized peritonitis are sought as already described. The Patient is asked to indicate the point of maximum pain – in appendicitis; this should correspond with McBurney's point (Pointing Sign). Classically there is right iliac fossa tenderness with grounding, again maximal at McBurney's point, and mild but persistent rigidity. If these symptoms are absent or equivocal, rebound tenderness can be elicited to gather with other signs of peritonitis. The appendix is retrocaecally cited in approximately 75% of cases. A partially or wholly retrocaecal appendicitis may present with symptoms and signs referable to the right flank and posterior aspect of the abdominal wall, lateral to the sacrospinalis muscle. The Patient is asked to roll over onto the left side tenderness may be elicited just medially to the right anterior superior iliac spine. The tenderness may be even higher with a high caecum, due to mmalrotation[28].

Other signs of peritonitis include Rovsing's sign. This is elicited by pressing in the left iliac fossa and the patient complaining of pain in the right iliac fossa. It is probably due to moving loops of the small bowel against the inflamed appendix in the right iliac fossa.The bowel sounds are auscultated as their absence confirms the suspicion of generalized peritonitis. Other signs that may be used full include the psoas test – where inflammation adjacent to the psoas muscles is diagnosed by active flexion of the right hip, giving rise to discomfort – or, in cases of psoas spasm, pain produced by hyperextending the hip with the Patient on their left side where inflammation is adjacent to the obturator internus, stretching this muscle by flexing and internally rotating the hip cases tenderness (Obturator test)[28].

Another useful sign in establishing the presence of local peritonitis is the shake test. Most surgeons performed this by grasping the iliac wings and shaking the pelvis from side to side. The patient complains pain at the appendix if local peritonitis is presentt[29]. A painful mass in the lower right quadrant may be palpable as the condition worsens. Although an abscess may be the source of a mass, it is also possible for the omentum and intestine loops to attach to an inflamed appendix.

INVESTIGATIONS

LABORATORY TESTS:

The majority of patient undergoing evaluation for acute abdominal pain has a complete blood count as a component of the evaluation. The leukocyte count is usually elevated to the range of 12000 to 18000 mm. In addition; an increase in the percentage of neutrophils (the “left shift”) with a normal total white blood cell count supports the clinical diagnosis of appendicitis. Other laboratory indices of inflammation have been studied as adjuncts to the diagnosis of appendicitis. C - reactive protein has been studied and correlated with the clinical and pathologic in general; this is not a clinically useful laboratory study because it is nonspecific. A urine analysis is often obtained in the evaluation of patients with abdominal pain to determine whether genitourinary tract inflammation is present. The urine analysis may show mild pyuria with appendicitis owing to the proximity of the ureter to the inflamed appendix[30].

RADIOLOGY

PLAIN RADIOGRAPHS

Prior to the widespread use of modern imaging techniques, plain abdominal films were often obtained in patients with abdominal pain, and a right lower quadrant faecolith (or appendicolith) was considered pathognomonic for acute appendicitis[31]. A calcified appendicolith is visible on plain films in only10% to 15% of patients with acute appendicitis. Studies show that faecoliths are not pathognomonic for appendicitis, as some patients with abdominal pain and faecolith have normal appendix.

In addition, faecoliths are not common enough in patients with appendicitis to be used as a reliable sign. As a result, plain abdominal radiographs are neither helpful nor cost-effective and are not recommended for the diagnosis of acute appendicitis. Plain erect abdominal x-rays are also useful for the detection of ureteral calculi, bowel obstruction, or perforations, but such conditions are unlikely to be confused with appendicitis[32].

ULTRASONOGRAPHY (USG)

Among patients with abdominal pain, Abdominal ultrasonography accounts for a sensitivity of 85% and a specificity of more than 90% in diagnosing the condition acute appendicitis[33].

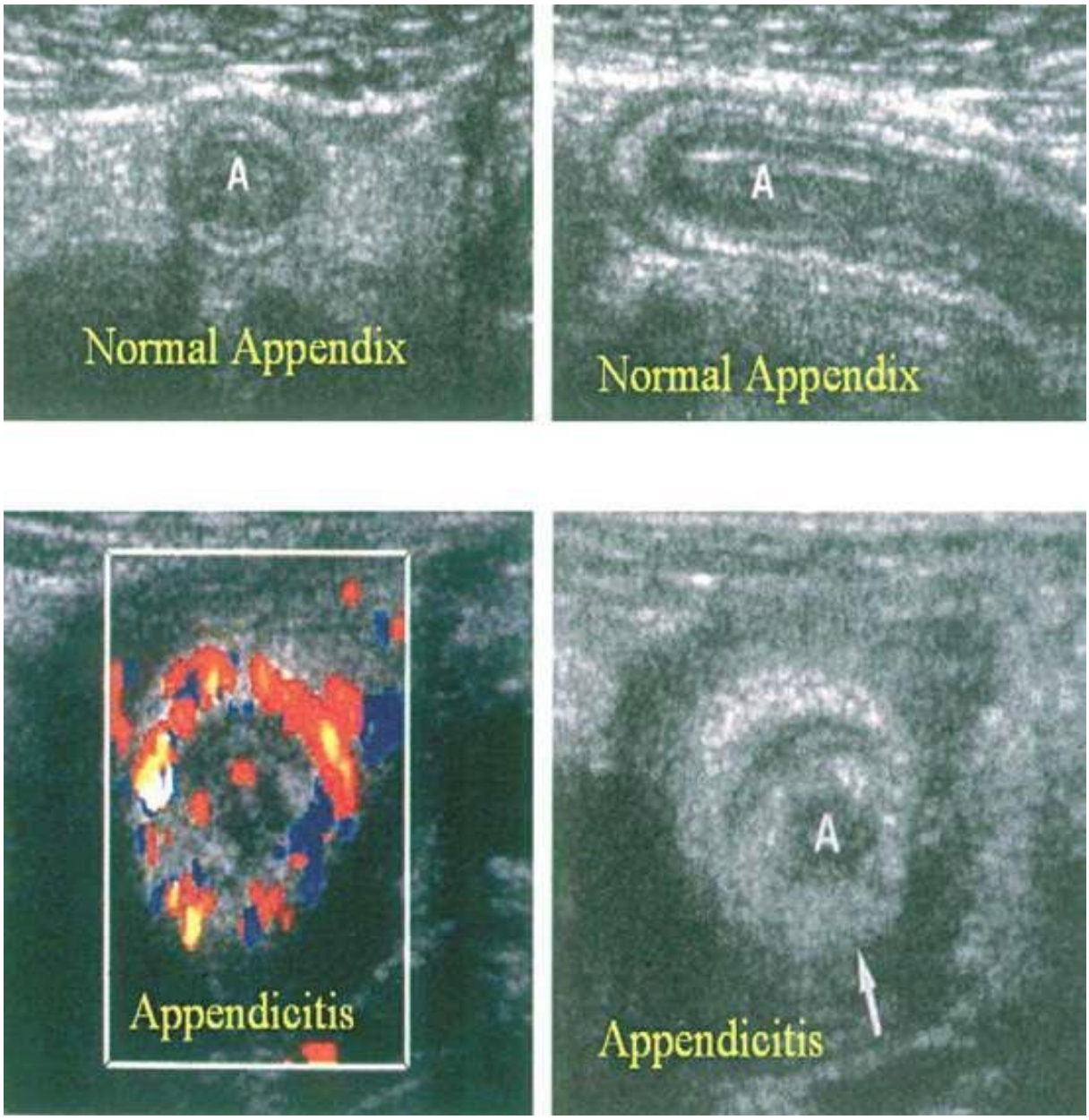


FIGURE 6: Ultrasonography images of appendix

Sonographic findings consistent with acute appendicitis include:

1. Appendix of seven mm or more in the anteroposterior diameter,

2. A thick-walled, noncompressible luminal structure seen in a cross-section referred to as a target lesion.

3. Increased echogenicity of the surrounding fat signifying inflammation, or

4. Presence of an appendicolith

5. In more advanced cases, peri-appendiceal fluid with or without mass.

Ultrasonography is preferred routinely as it is a noninvasive modality that requires no prior patient preparation that also avoids exposure to radiation. Thus, it is commonly used in children and in pregnant patients with equivocal clinical findings suggestive of acute appendicitis. The disadvantage of ultrasonography is that it is highly operator-dependent, and it is frequently unable to visualize the normal appendix. Pelvic ultrasound can be especially useful in excluding pelvic pathologies, such as a tubo-ovarian abscess or ovarian torsion, that may mimic acute appendicitis[34].

COMPUTED TOMOGRAPHY (CT):

CT signs of appendicitis include an appendix measuring greater then 6 mm in diameter, failure of the appendix to fill with oral contrast or air up its tip, an appendicolith. And enhancement of its wall with intravenous contrast. Surrounding inflammatory changes include increased fat attenuation, fluid, inflammatory phlegmon, caecal thickening abscess, extraluminal gas and lymph-adenopathy. Sometimes the lumen of the caecum can be seen pointing toward the obstructed opening to the appendix (the 'arrow–head' sign). A normal appendix is more frequently seen on CT than at an ultrasound. Sensitivity and specificity are approaching 100%[35].

DIAGNOSTIC LAPAROSCOPY:

This investigation has a useful role in the equivocal case of appendicitis. An interesting study by Patterson-Brown and his associates showed that after laparoscopy, only 3 out of 40 patients (7.5%) had an unnecessary appendicectomy compared with 11 of 60 patients (22%) operated on without this investigation. This was particularly useful in female patients. Excellent results, of course, can only be obtained under ideal conditions. If the widespread use of

laparoscopy is to be advocated as an essential investigation in the management of the acute abdomen, general surgeons require training to become expert laparoscopists[36].

ALVARADO SCORE:

A number of clinical and laboratory-based scoring systems have been devised to assist in diagnosis. The most widely used clinical scoring is the Alvarado score.

Symptoms	**Score**
Migratory RIF pain	1
Anorexia	1
Nausea & vomiting	1
Signs	
Tenderness in RIF	2
Rebound tenderness in RIF	1
Elevated temperature	1
Laboratory findings	
Leucocytosis	2
Shift to left	1
Total	**10**

TABLE 2- Components of the Alvarado scoring system

Interpretation

· Score 7-10: High probability of acute appendicitis

· Score 4-6: Equivocal probability of acute appendicitis

· Score 1-3: Unlikely of acute appendicitis[37]

This scoring system is simple to apply in clinical use and easy to assess. Thus, it can be performed even on the patients attending the outpatient unit.

HISTORY OF PLATELETS

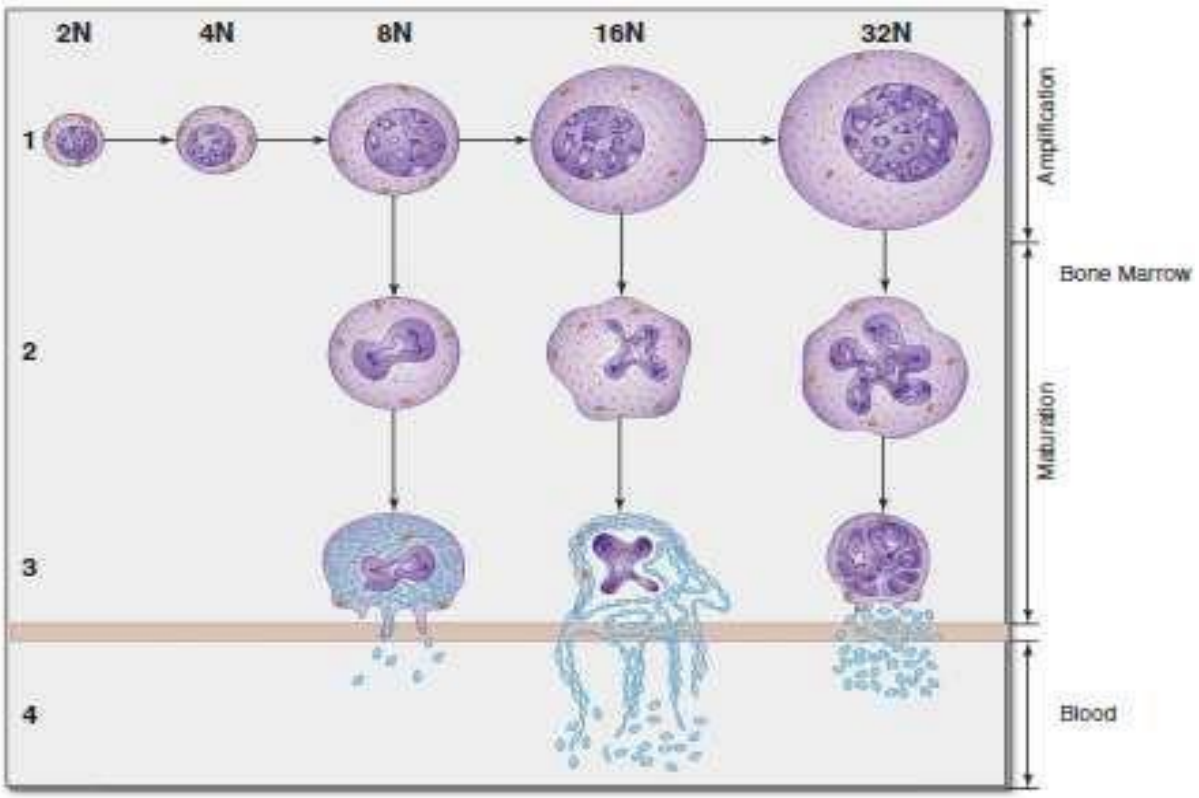
Many eminent researchers have been honoured for being the first to name and characterise the blood platelet. Osler, one of them, identified disk-like objects that flowed throughout the blood stream and accumulated upon removal in papers he published in 1873[38]. In 1882, Bizzozero examined them under a microscope in the blood that was being circulated in living creatures and in blood that had been drawn from blood vessels, demonstrating that they were the first blood component to cling to injured blood vessel walls both in vivo and in vitro. Then, Osler continued his research to show that blood platelets play a part in thrombotic illness, referring to these blood plaques as "atheromatous ulcers" on heart valves and aortic aneurysms. Megakaryocytes produce discoid, nucleus-less cellular fragments called blood platelets[39]. Platelets typically have a diameter of 2 to 3 m, and the average lifespan in humans is about 10 days. 40 Human platelet counts typically range from 150,000 to 400,000/l, however spontaneous bleeding due to diminished (but functionally normal) platelets is uncommon at levels beyond 10,000/l.

PLATELET FORMATION:

Megakaryocytes (MKs) are progenitor cells that are highly specialised for producing and releasing platelets into the bloodstream. Megakaryopoiesis is the term used to describe the genesis of megakaryocytes. The earliest recognised cell in this lineage is the megakaryoblast, which passes through a sequence of endomitoses to develop into a megakaryocyte at the 16N stage, as shown in Fig.7.

Megakaryocyte cytoplasm fragments break down to produce platelets. A group of them known as proplatelets appears to be released from the megakaryocytes' membrane extensions, producing mature platelets as shown in Fig 7.

FIGURE 7: Megakaryopoiesis



PLATELET LIFE SPAN

Typically, platelets circulate in the blood for 7 to 10 days at a time. Senescence or random removal of a defined fraction of platelets up to 7.1x109/l/day in endothelium supportive activities are the two processes by which platelets are lost from circulation. Although the greater blood flow through the liver enables severely damaged platelets to be eliminated more quickly by hepatic macrophages, senescent platelets are largely removed by macrophages in the spleen. Aging platelets are thought to have lower levels of sialic acid and more surface IgG[41].

LIGHT MICROSCOPY

Wright-stained smears under a light microscope show that platelets are tiny, anucleate pieces with sporadic reddish granules, measuring about 2 m in diameter with a volume of around 8 fl[42,43] and showing significant variation in size and form.

PLATELET CYTOSKELETON

The cytoskeleton, which is made up of monomers, filaments, and tubules, controls platelet shape change, extracellular extensions, the collection and extrusion of secretory granules, and surface activity. Platelets' ability to contract and spread as well as their ability to change shape are all dependent on the cytoskeleton. Three different structures carry out these various tasks: first, the membrane skeleton, which supports the inner side of the plasma membrane; second, the mass of actin and intermediate filaments, which fills the cytoplasm (cytoplasmic actin filaments; also known as the sol-gel zone); and third, the circumferential microtubule band, which wraps the platelet's substance to create the resting disclike form[44,45].

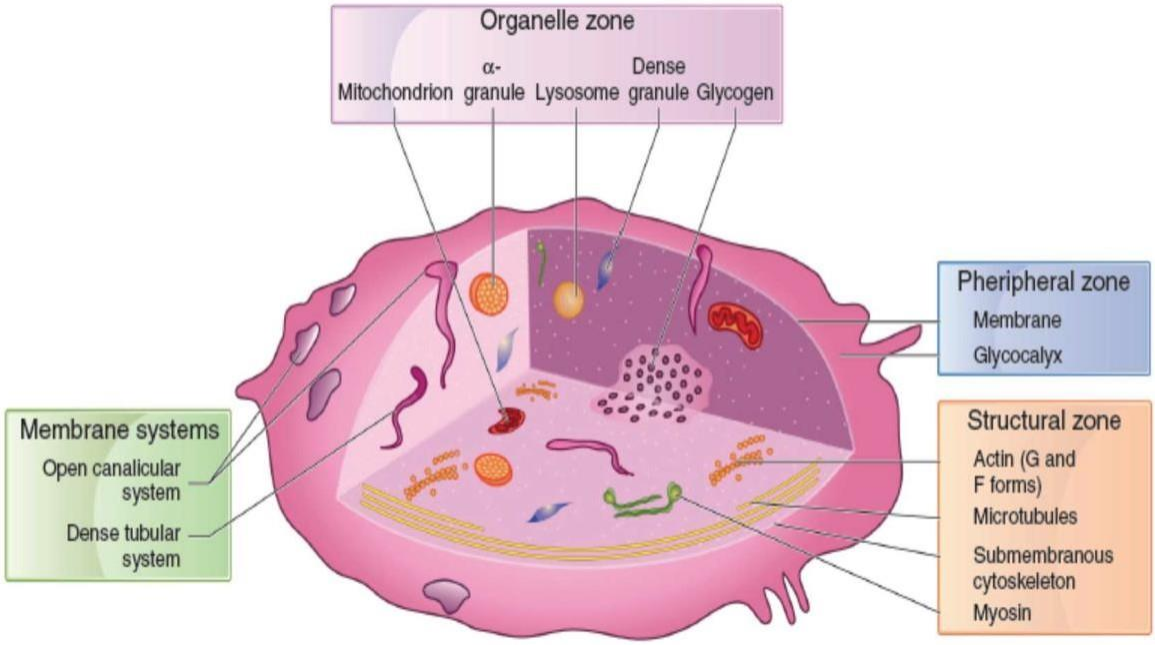


FIGURE 8: Structure of Platelet

PLATELET GRANULES AND ORGANELLES

(a) PLATELET GRANULES

Any given stimulus appears to need to be amplified or accented in order for normal platelet activity to occur. As a result, platelets have secretory granules and mechanisms that do this by releasing extra stimulatory substances that were previously locked away inside the resting platelet. The dense bodies and the -granules, two major secretory granules, appear to be the primary effectors due to their highly reactive and easily accessible contents [i.e. fibrinogen and adenosine diphosphate (ADP)]. A wave of calcium release triggers a sharp rise in platelet metabolic activity, which is accompanied by an increase in adenosine phosphate (ATP) synthesis. This activity is the precursor to platelet granule secretion[46,47].

(b) ORGANELLES: MICROPEROXISOMES, COATED VESICLES, MITOCHONDRIA, AND GLYCOGEN

The structure may contribute to the synthesis of platelet-activating factor, but its ultimate fate within the platelet cytoplasm is unknown[48]. Coated vesicles are rare, small (90 nm in diameter) granules that can be identified by their electron-dense bristle coat. Microperoxisomes are rare, small (90 nm in diameter) granules that are demonstrable with alkaline diaminobenzidine. The coated pits and vesicles themselves contain the same clathrin surface coat that is present in the plasma and SCCS membrane, according to special staining[49].

With the exception of their reduced size, platelet mitochondria are comparable to those in other cell types. There are roughly seven of them per human platelet, and they are where the citric acid cycle and the respiratory chain function. Glycogen is a substance that plays a crucial part in platelet metabolism and is present in minute particles or in masses of closely related particles[50].

PLATELET FUNCTION

Platelets perform a variety of tasks, such as adhesion, spreading and changing shape, aggregation, secretion, procoagulant activity, and clot retraction.

ADHESION: Following vascular injury, platelet adhesion to exposed subendothelial matrix proteins is the initial event. The platelet glycoprotein receptors that control adhesion rely on the shear rate. Circulating platelets are drawn into the thrombus through adhesion as well[51].

SHAPE CHANGE AND SPREADING: In order to connect with other platelets and the vessel wall, activated platelets grow spherical and extend pseudopodia. The word "shape change" refers to the transition to a sphere, which increases their optical density. However, this term should only

be used when validated by scanning electron microscopy because an increase in density can also be achieved in other ways. Myosin light chains are phosphorylated to change their shape. This can happen either as a result of an increase in intracellular Ca2+ ions, which activate myosin light chain kinase, or by inhibiting myosin light chain phosphatase, which is controlled by Rho kinase and functions downstream of it[51].

AGGREGATION: The term "aggregation" refers to the cross-linking of platelets caused by fibrinogen or other bivalent or multivalent ligands like vWF binding to the integrin IIb3 on neighbouring cells[51].

SECRETION: The three different types of granules each have a unique combination of components that contribute differently to haemostasis. A variety of secretory illnesses that are linked to excessive bleeding are caused by a lack in dense or -granules[51].

PROCOAGULANT ACTIVITY: One important role of platelet activation is to provide a negatively charged phospholipid surface for the construction of the tenase and prothrombinase complexes, two multiprotein complexes that are essential components of the coagulation cascade. The development of the negatively charged lipid surface on active platelets is frequently referred to as procoagulant activity or antiphospholipid exposure. Phosphatidyl serine moves from the inner to the outer leaflet of the platelet membrane to create it[51].

PLATELET-DERIVED MICROPARTICLES: When platelets are activated, platelet-derived microparticles are produced, and they are typically observed together with an increase in procoagulant activity. In order for platelet microparticles to develop after receptor activation,

substantial agonist concentrations and favourable circumstances are needed. Platelet microparticle formation also necessitates Ca2+ entrance and is easily observed in response to stimulation by Ca2+ ionophore[51].

CLOT RETRACTION: Clot retraction, the process through which blood clots shrink over a period of minutes to hours, has been recognised for more than two centuries. The strong shear stresses present in small arterioles and other arteries are made tolerable for platelet-rich thrombi by this occurrence. By sampling aliquots of the volume of plasma over time after adding thrombin, it is simple to assess the amount of clot retraction in platelet-rich plasma triggered by thrombin. Thrombin quickly forms a blood clot that fills an aggregometer tube, but over the course of 60 minutes, it progressively shrinks to approximately 20% of its initial volume[51].

PLATELET INDICES

Automation in haematology has made it possible for researchers to measure more recent factors besides platelet count, such as platelet indices. Additional information on the morphology and maturity of the platelets is valuable thanks to these platelet indicators. Researchers are looking more closely at the platelet indices plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) in a variety of clinical conditions. When well defined and accurate, the laboratory-based reference ranges can be crucial for understanding the results and potentially save needless, expensive follow-ups. A widely used tool is the measurement of platelet count in peripheral blood. The mean platelet volume (MPV) and platelet distribution width are the two most often utilised indices that have been derived from platelets similarly to RBC (PDW). Numerous platelet parameters, including PDW, MPV, PCT, and P-LCR, may now be measured thanks to recent developments in automated blood cell analysers. These measures offer some useful data but have not yet been recognised for normal clinical usage[52].

MEAN PLATELET VOLUME (MPV) Unless the platelet count is exceptionally low, measuring peripheral blood platelet counts does not provide much information about platelet-related haemostatic function. The mean platelet volume, a platelet parameter that can provide useful clinical and patho-physiological information regarding patients and vascular illnesses, is measured by the majority of haematology analyzers[53].

PHYSIOLOGY OF PLATELET SIZE

MPV seems to be a factor or potentially a sign of platelet function. In vitro, larger platelets are more reactive than smaller ones. They produce more prothrombotic and vasoactive factors, such as arachidonic acid metabolites (such as Thromboxane A2), serotonin, thromboglobulin, and ATP, have more dense granules, and have higher LDH activity. They preferentially and more quickly aggregate to platelet agonist including ADP, collagen, and adrenaline[8]. They are linked to a shorter bleeding time (BT; a measure of in vivo haemostatic function)[7]. Whether assessed in platelet rich plasma or whole blood, populations of patients, or in some disease situations, such as diabetes, MPV correlates with platelet aggregation. a type of diabetes. Adhesion molecules are expressed at higher amounts in large platelets as well. Eg. P-selectin, GPIIb/IIIa, despite the fact that their surface densities often remain constant regardless of platelet volume[53].

THE MEGAKARYOCYTE-PLATELET-HAEMOSTATIC AXIS:

Because platelets are anucleate cells, they have a limited or nonexistent potential to synthesise proteins. Regarding size, density, and hemostatic capability, platelets vary widely. Previously, it was believed that platelet size declined with ageing; however, more recent research indicates that MPV, other platelet characteristics, and therefore platelet protein content and reactivity, are predominantly determined at or prior to thrombopoiesis by the MK, the platelet

precursor cell. MKs stand apart from other mammalian cells because they are polyploid. That is to say, they can undergo endomitosis, or the duplication of chromosomal DNA, without undergoing subsequent full mitotic cell division. With 16N being the modal ploidy in the majority of mammals so far studied, MKs go through different numbers of endomitotic cycles to form a population of cells whose ploidy spans from 4N to 128N (where 2N represents the typical diploid state). Each MK generates between 1000 and 2000 platelets, most likely as a result of cytoplasmic fragmentation in the pulmonary circulation[54]. Megakaryocyte-platelet haemostatic axis measurements in humans indicate that platelet and MK characteristics are so closely related that they can be treated as a single system (MPHA). For instance, in healthy people, platelet count and MPV have an inverse relationship; platelet mass, which is the result of MPV and platelet count, is nearly constant; platelet mass corresponds with BT; and BT has an inverse relationship with MK ploidy and size. When acute platelet destruction takes place in the absence of platelet production, MPV rises but MK ploidy stays the same; when platelet production rises on its own, MK ploidy rises; and when acute platelet destruction and platelet production co-occur, MPV and MK ploidy rise simultaneously. Therefore, it would seem that MPV and MK ploidy can change jointly or separately in response to different haemostatic demands. Due of this, it has been hypothesised that MPV and MK ploidy regulation, and consequently platelet count, are controlled by distinct hormonal systems. Variations in MPV occur from changes in the rate of platelet oxidation, whereas changing MK ploidy, together with concurrent changes in MK size and cytoplasmic volume, are connected to changes in the pace of platelet formation[54].

MEASUREMENT OF PLATELET VOLUME

When a platelet passes through a small aperture, the best technique for determining platelet volume takes advantage of variations in either electrical impedance (as used in Coulter haematology analyzers) or light diffraction (as used by Technicon). Alternative, less effective techniques include flow cytometry or semi-quantitative diameter measuring on platelet smears[53].

In the Coulter series, fluid-assisted cells are flown through a small aperture, resulting in a change in voltage inversely proportional to the size of the particles. A raw histogram is produced, and the data is then fitted with a log-normal curve. Together with the MPV, which is estimated using numerical integration, platelet count is generated from this. Similar to the Sysmex, which also uses cells suspended in fluid to monitor parameters, the Sysmex focuses the cells hydrodynamically such that they pass through the aperture in a straight line. This stops cells from passing through the aperture's edge and inadvertently altering the electrical field. The top and lower discriminators are both movable, which is another way in which it varies from Coulter. As a result, the distribution curve obtained is not a fitted curve but rather the real data. By applying the formula MPV (fL)=Pct (%)x1000Plt (x103/L), MPV may be derived from the curve.

The size and granularity of cells in suspension are measured using Technicon devices, which utilise laser-optic technology. When a beam of light passes through cells, the amount of forward scatter relates to the size of the particles, but the amount of side scatter relates to density or granularity. The data are converted into a platelet histogram, and MPV is computed as the mode. When Coulter and Technicon data were compared, differences of up to 40% were discovered. Typically, EDTA is used to anticoagulate complete blood count specimens, which causes platelets to enlarge in a time-dependent way. The first 1.5 hours are when MPV increases the most, but the process continues over the following 24 hours. EDTA is hypothesised to alter plasma membrane permeability and raise intracellular cyclic AMP. This problem is made more challenging by the fact that analyzers that use light diffraction determine particle size by evaluating optical density. Since platelet swelling causes a decrease in optical density, these analysers detect a decreasing MPV with time. Therefore, unless MPV is measured at a consistent point after phlebotomy or once the edoema has subsided at 24 hrs, studies reporting raw MPV readings made in EDTA are of uncertain clinical or research significance. A high concentration of sodium citrate is used to assess MPV, which does not fluctuate with time143 and is hence regarded as the gold standard.

PLATELET DISTRIBUTION WIDTH (PDW)

It is a quantitative measurement of platelet size and volume, and its utility in differentiating between reactive and essential thrombocytosis is limited. In the presence of platelet anisocytosis, PDW increases. Although the typical range for platelet volume has not yet been fully established, research evaluating PDW in sodium citrate in healthy persons indicate that it is between 10.0% and 17.9% on average[55]. In a prospective investigation on platelet distribution width in thrombocytopenia, Reddy S. R. et al. discovered that PDW is a crucial index in platelet characteristics. It can provide important details about the mechanism of platelet destruction, coupled with other platelet indices. According to the method that caused them, cases with low platelet counts were divided into three main categories: increased destruction, decreased production, and splenic sequestration/abnormal pooling. Platelet heterogenicity and destruction were both associated with higher variation in platelet distribution width (PDW), and PDW varies inversely with platelet destruction in splenic pooling[54].

According to a study by Borkataky et al.[57] on platelet volume indices, people with destructive thrombocytopenia (malaria, leishmaniasis, and dengue fever) have higher MPV levels than people with hypoproliferative thrombocytopenia. Additionally, it has been discovered that destructive thrombocytopenia has higher PDW and PLCR levels than hypoproliferative thrombocytopenia[57].

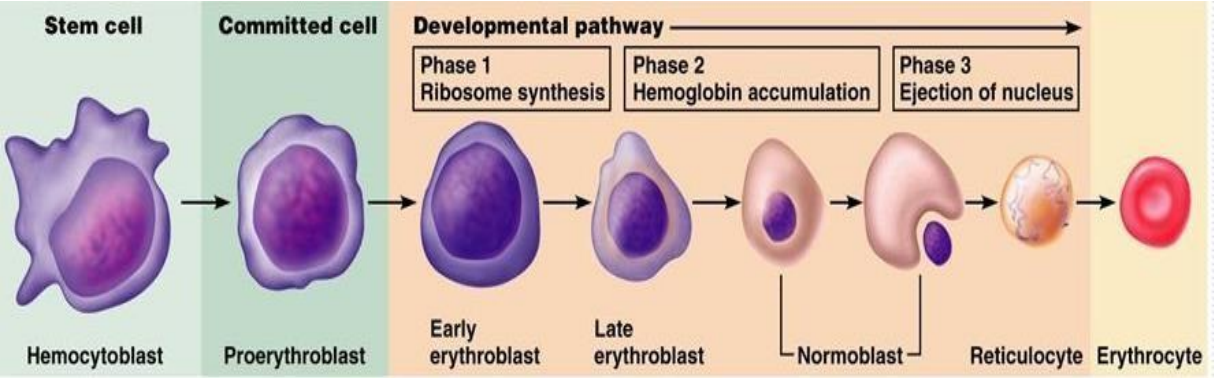
HISTORY OF RED BLOOD CELL

Phlebotomy has been performed with the naked eye since very early times. The examination of the blood's composition was made possible by Hans and Zacharias Jannsen's invention of the compound microscope in Holland around 1590. Red blood cells were first observed under a microscope in 1658 by Dutch naturalist Jan Swammerdam (1637-1680). Swammerdam's friend and fellow Dutch microscopist Antoni van Leeuwenhoek (1632–1723) defined the dimensions and shape of "red corpuscles" and created the first picture of them in 1695[58]. If anyone examined blood under a microscope over the following 150 years, only the "red corpuscles" were visible.

ERYTHROPOIESIS

The final stage of erythropoiesis begins in the bone marrow and happens in the blood. Multipotent hematopoietic stem cells are used to become mature red blood cells, which then undergo a lengthy maturation process including numerous morphological changes to become highly functional specialised cells. The last stages in mammals entailed the nucleus being ejected from erythroblasts, which resulted in the development of reticulocytes. Organelles and ribosomes are selectively removed from reticulocytes in addition to plasma membrane modification in order to form mature biconcave red blood cells. The mechanisms behind these final stages of maturation are currently being studied. Dramatic chromatin condensation and the creation of nuclear polarity during enucleation are caused by a rearrangement of the actin cytoskeleton and the production of vacuoles at the nucleus-cytoplasmic interface, which is clathrin-dependent. The interaction of erythroblasts and macrophages at the erythroblastic island favours this process. Mitophagy is the process of removing mitochondria. This macroautophagy mechanism involves the destruction of mitochondria by engulfing them in an autophagosome, a double-membrane structure.

FIGURE 9: Erythropoiesis



LIFESPAN

After developing from erythroblasts in the bone marrow, human red blood cells (RBC) are discharged into the blood and remain in the circulation for around 115 days. RBC typically survive in a non-random fashion in humans and certain other mammals. This indicates that the reticuloendothelial system removes every RBC within a certain age cohort at around the same time. In reality, there is a big difference in the longevity of human RBC. This value may range from 70 to 140 days in a healthy person with a mean RBC lifespan of 115 days[59]. The average lifespan of people varies by about 15% among them.

CYTOSKELETON

Several proteins make up the erythrocyte cytoskeleton, which forms a filamentous network beneath the lipid bilayer. Actin, spectrin, ankyrin, and protein 4.1 make up the network. To preserve the integrity of the membrane, cytoskeletal proteins interact with the essential lipids and proteins of the bilayer. Shape, flexibility, and lipid structure of the erythrocyte are significantly influenced by the cytoskeleton. Spectrin is the predominant membrane protein in terms of both size and copies per erythrocyte. Two proteins with molecular weights of 240,000

and 220,000 daltons make up this substance. To create heterodimers, both proteins are twisted together into long, flexible structures[28]. Heterodimers "head-to-head" interact to generate tetramers and possibly higher order oligomers. Actin forms a series of polygons (usually hexagons) with spectrin tetramers as the sides when it binds to the "tail" of many heterodimers.

Actin-spectrin interaction is encouraged and maybe regulated by membrane protein 4.1. Just below the lipid bilayer is the net-like structure created by the protein-protein interactions of spectrin, actin, and protein 4.1. It is connected to the bilayer's proteins and lipids in at least three different ways. A link from the network to the membrane protein is formed when ankyrin, another cytoskeleton protein, attaches close to the centre of the spectrin tetramers. The cytoskeleton and glycophorin, another transmembrane protein, are connected in 4.1. Polyphoinositid may be able to alter that connection[60].

RED CELL DISTRIBUTION WIDTH (RDW)

For the differential diagnosis of anaemia, red blood cell distribution width (RDW), a numerical representation of the heterogeneity of red blood cell (RBC) size and volume, has been utilised extensively. A typical aspect of a complete blood count (CBC) that is frequently utilised in emergency rooms is red blood cell distribution width (RDW), which is calculated as a percentage of the number of circulating red blood cells that deviate from the mean volume.

Recent research has linked RDW closely to the development, course, or prognosis of a number of inflammatory disorders, including systemic lupus erythematosus, Sjögren syndrome, systemic sclerosis, and cardiovascular disease. Additionally, a study in an unselected outpatient population demonstrates a favourable connection between RDW and inflammatory indices including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)[61]. Therefore, it has been hypothesised that RDW may be a novel inflammation index and that an increase in RDW may

indicate that the body is inflammatory. Any illness event that results in the early release of reticulocytes into the circulation might lead to elevated RDW.

It is calculated as a percentage of the standard deviation of the red cell volume divided by the mean corpuscular volume[61].

In order to identify iron deficiency anaemia from other microcytic anemias, RDW is often employed in haematology practise. Erythropoiesis dysfunction or erythrocyte destruction are linked to higher RDW.

Inflammatory and infectious illnesses such rheumatoid arthritis, inflammatory bowel disease, colon cancer, and celiac disease have also been studied using RDW. Increased levels of inflammatory markers such C-reactive protein (CRP), erythrocyte sedimentation rate, and interleukin-6 have been demonstrated to be linked to RDW increases. Proinflammatory cytokines decrease erythrocyte maturation and shorten the life span of circulating erythrocytes in sepsis. Additionally, it has been discovered that RDW level is a predictor of mortality in bacteremia and septic shock[60].

It has been demonstrated that the proinflammatory cytokines of sepsis (tumour necrosis factor A, interleukin 6, and interleukin 1b) directly and adversely affect red blood cell survival in the circulation, encourage membrane deformability, and inhibit erythrocyte maturation. Thus, these sepsis-related inflammatory mediators may encourage the entry of more recent, bigger reticulocytes into the peripheral circulation, increasing RDW.

According to research, inflammatory mediators decrease erythrocyte maturation, which affects red blood cell survival in the circulation and increases RDW by allowing for the entry of newer, larger reticulocytes into the peripheral circulation[61].

MATERIAL AND METHODS

STUDY DESIGN:

- Prospective Observational Study.

SOURCE OF DATA:

- All patients admitted with the clinical diagnosis of acute appendicitis and its complications in the department of general surgery of B.L.D.E(Deemed to be University) Shri B.M. Patil Medical College, Hospital, and Research Centre.
- The period of study is from January 2021 to November 2022.

METHOD OF COLLECTION OF DATA:

- Diagnosis of acute appendicitis will be made on the basis of thorough clinical examination, appropriate laboratory, and radiological investigations.
- Venous blood samples were collected in di-potassium EDTA tubes.
- The samples were run within two hours of venepuncture using the 6 part differentiated automated Hematoanalyzer (Sysmex XN-1000) and complete blood count analysis of the samples including the platelet indices (MPV, PDW, PCT and P-LCR) was performed in the study group and the control group.
- A pretested structural pro forma will be used to collect relevant information for each individual patient.
- Data will be recorded on the master chart for analysis.

- Written informed consent will be obtained from all the patients.

Cases will be selected consequently with the following inclusion and exclusion criteria.

INCLUSION CRITERIA:

- All patients clinically diagnosed with acute appendicitis on admission and confirmed by ultrasonography / computed tomography.
- All patients clinically diagnosed with appendicular perforation on admission.
    - For both these groups, who underwent appendicectomy and with confirmed histopathological report, suggestive of appendicitis would be included.

EXCLUSION CRITERIA:

- All patients diagnosed with appendicular mass and treated conservatively.
- All patients with hemolytic disease.
- All patients with bleeding and platelet disorder.
- All patients on drugs which alter coagulation profile and platelet count.

SAMPLE SIZE:

Based on a study done by Craig S et al. in 2014[76], with an anticipated incidence of acute appendicitis of 10 per lakh population (01%), the study would require a sample size of **190 patients** with a 95% level of confidence and 2% absolute precision.

Formula used:

- $n=\frac{z^2\ p*q}{d^2}$

Where Z= Z statistic at α level of significance

d2= Absolute error

P= Proportion rate

q= 100-p

SAMPLE SIZE: 190 patients

STATISTICAL ANALYSIS:

- The data obtained will be entered in a Microsoft Excel sheet, and statistical analysis will be performed using a statistical package for the social sciences (Version 20).
- Results will be presented as Mean (Median) ±SD, counts and percentages, and diagrams.
- More than two groups will be compared using ANOVA/Kruskal-Wallis test.
- The diagnostic value of laboratory parameters that predict the presence of acute appendicitis will be calculated using receiver operating characteristic (ROC) curve analysis.

INVESTIGATIONS / INTERVENTIONS:

Investigations or Interventions required in this study are routine, standardized procedures. There are no animal experiments involved in this study.

These investigations are required as routine before taking any patient for appendicectomy are:

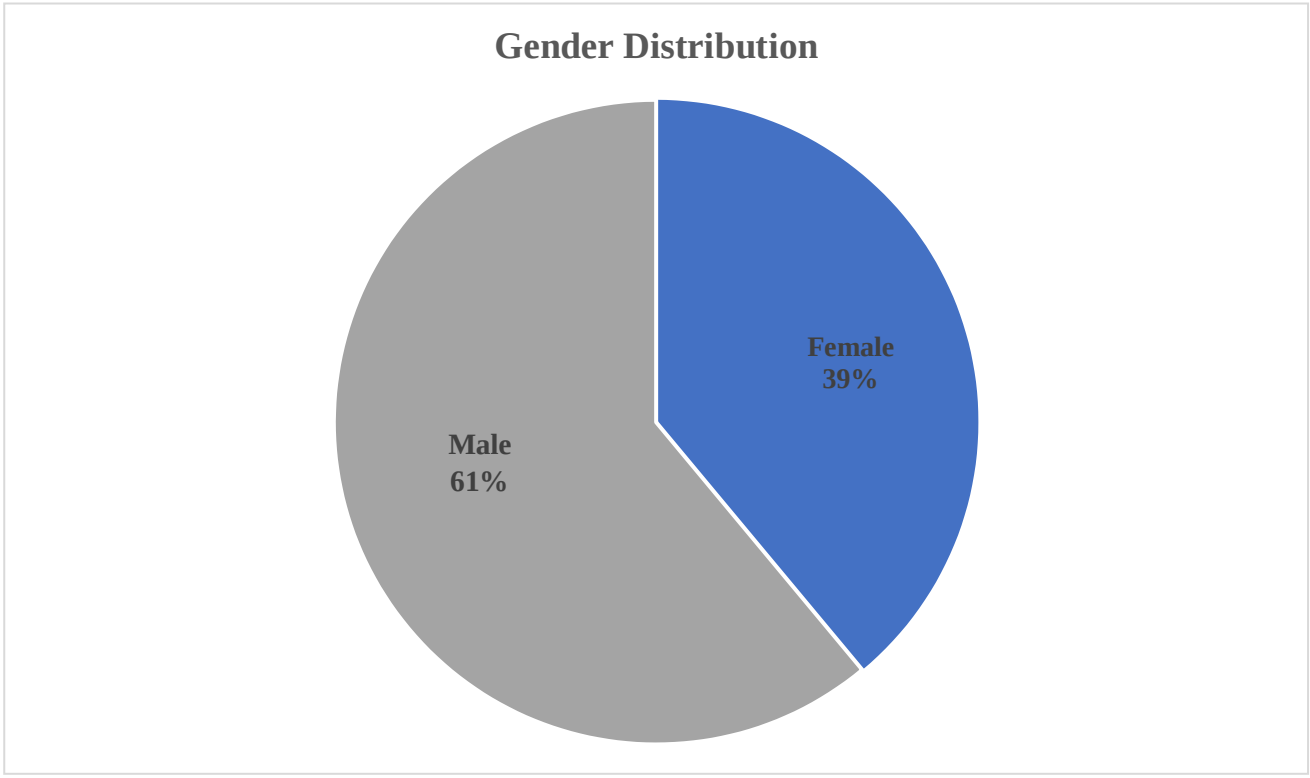
- Complete blood count- total leucocyte count, differential leukocyte count,
- platelet count, PDW, MPV, and RDW.
- Bleeding and clotting time.
- Urine – sugar, albumin, and microscopy.
- Random blood sugar, Blood urea, Serum creatinine.
- Electro-cardio-gram and Chest X-ray.
- Human Immunodeficiency Virus, Hepatitis B virus.
- Ultrasonography / computed tomography of abdomen and pelvis.

RESULTS

TABLE 3: DISTRIBUTION OF CASES ACCORDING TO GENDER

Gender	Number of Cases	Percentage (%)
Female	74	39
Male	116	61
Total	**190**	**100.0**

FIGURE 10: PIE CHART SHOWING DISTRIBUTION OF GENDER



Age Interval	Frequency	Percent
< 10	3	1.6
10 - 19	53	27.9
20 - 29	63	33.2
30 - 39	40	21.1
40 - 49	10	5.3
50 - 59	10	5.3
60 - 69	8	4.2
70+	3	1.6
Total	190	100.0

TABLE 4: CASE DISTRIBUTION ACCORDING TO AGE INTERVAL

FIGURE 11: BAR GRAPH SHOWING DISTRIBUTION OF CASES ACCORDING TO AGE

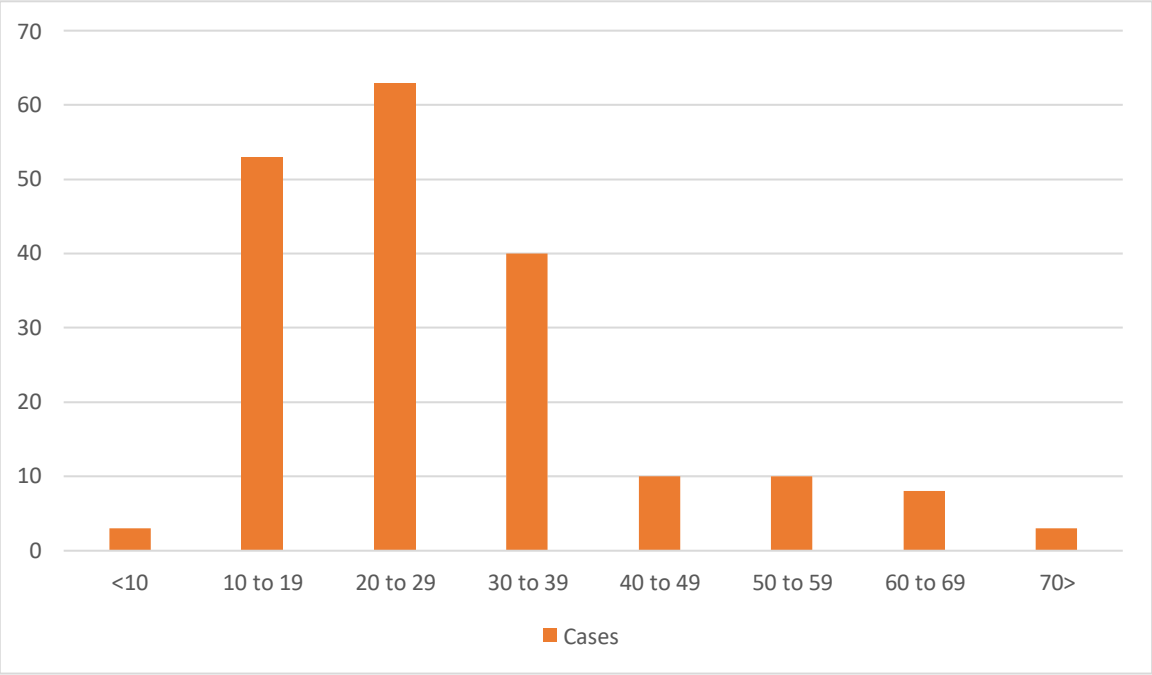


TABLE 5: DISTRIBUTION OF MEAN OF VARIOUS HEMATOLOGICAL PARAMETERS BETWEEN THE ACUTE APPENDICITIES AND PERFORATED APPENDICITIES

Note: * significant at 5% level of significance ($p<0.05$)

Parameters	Acute (n=169)		Perforated (n=21)		p-value
	Mean	±SD	Mean	±SD	
Total count	10475.62	3846.59	13947.19	7376.32	0.026*
Platelet count	283.89	70.19	311.33	154.37	0.440
PDW	11.60	1.91	10.92	2.47	0.036*
MPV	9.27	1.06	8.47	1.26	0.002*
RDW	14.71	1.64	15.61	2.81	0.442

FIGURE 12: BAR GRAPH SHOWING DISTRIBUTION OF MEAN OF VARIOUS HEMATOLOGICAL PARAMETERS BETWEEN THE ACUTE APPENDICITIES AND PERFORATED APPENDICITIES

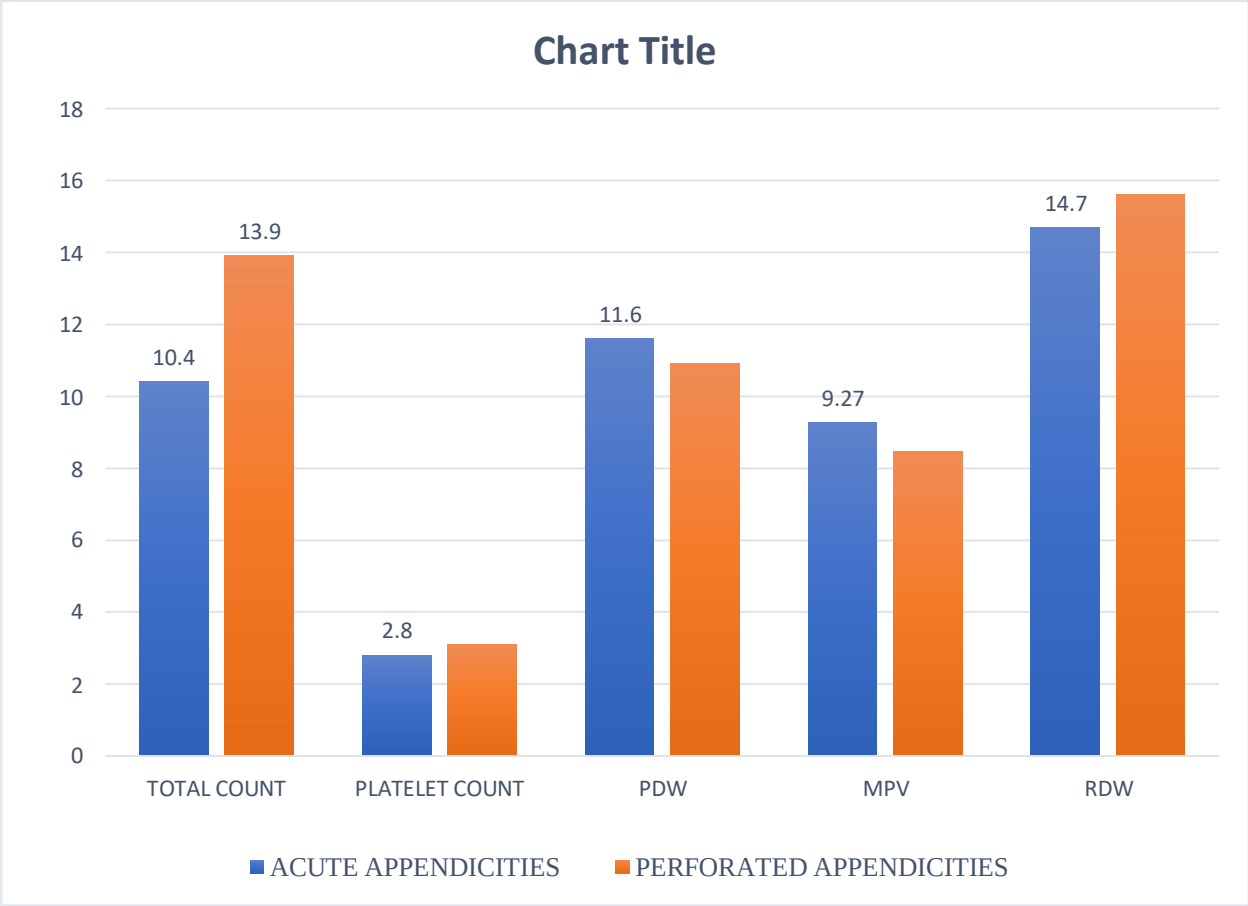
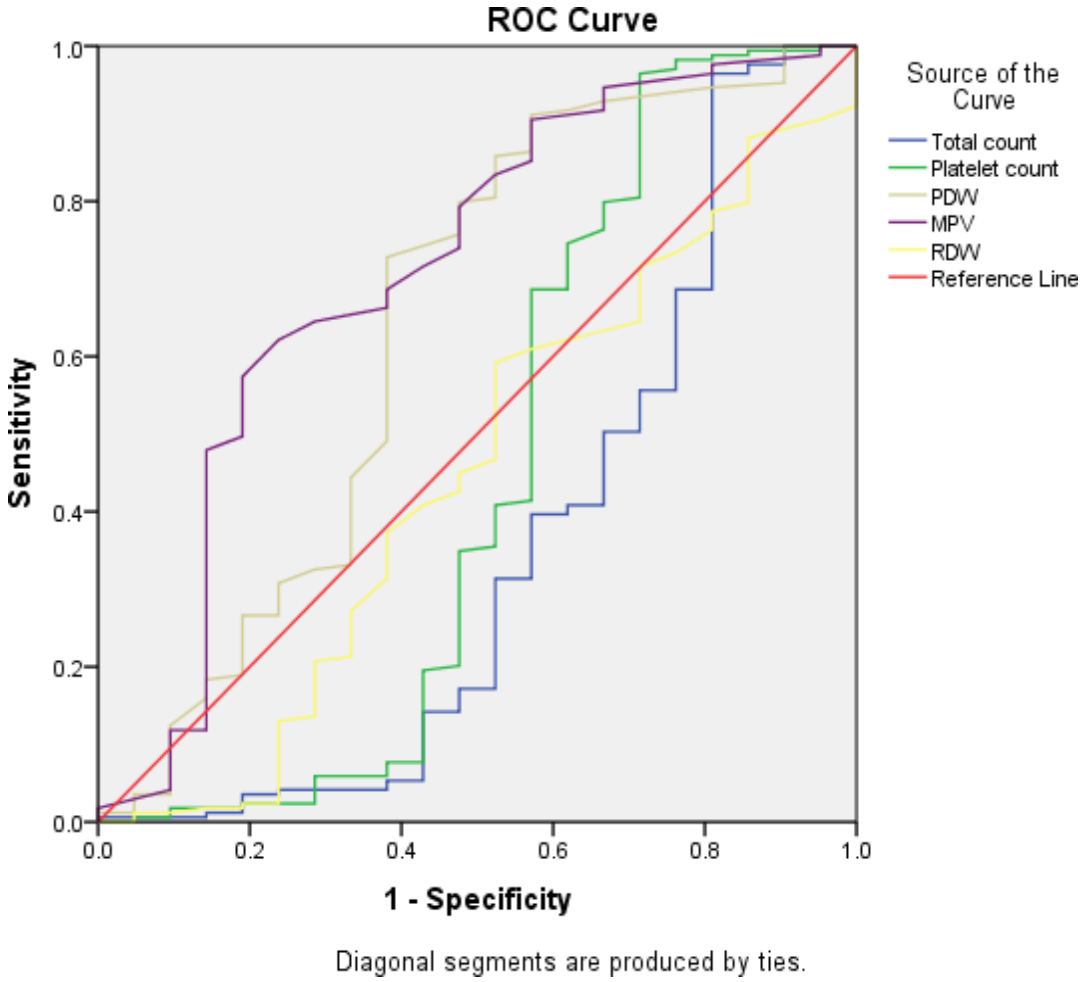


TABLE 6: ROC CURVE ANALYSIS OF ALL PARAMETERS IN PREDICTING ACUTE APPENDICITIS AND PERFORATION

Note: * significant at 5% level of significance (p<0.05)

Parameter	Area	Standard Error	Asymptotic 95% Confidence Interval		p value	Cut-off Value	Sensitivity	Specificity
			Lower Bound	Upper Bound				
Total count	0.351	0.081	0,191	0.510	0.026*	>5300 /L	96.5%	19%
Platelet count	0.448	0.092	0.268	0.628	0.440	>169 x 10^9 /L	96%	29%
PDW	0.641	0.078	0.488	0.793	0.036*	<10.45 fL	73%	62%
MPV	0.711	0.069	0.576	0.845	0.002*	<9.05 fL	57%	81%
RDW	0.449	0.073	0.306	0.591	0.442	>14.15 %	59%	48%

FIGURE 13: ROC CURVE ANALYSIS SHOWING ALL PARAMETERS IN PREDICTING ACUTE APPENDICITIS AND PERFORATION



DISCUSSION

Around the world, acute appendicitis is still a common abdominal emergency. Early and accurate diagnosis of acute appendicitis is required to reduce the morbidity and mortality linked to delayed diagnosis and its complications. Negative appendectomy is also responsible for the loss of important time for medical staff and financial resources, in addition to significant morbidity and death[62].

The diagnosis of acute appendicitis remains a diagnostic challenge for clinicians despite significant advancements in the diagnostic field and the development of sophisticated examinations. USG and/or CT scan investigations cannot reliably identify acute appendicitis. The clinical diagnosis is still debatable because acute appendicitis can show in a variety of ways and there aren't many trustworthy diagnostic tests available. As was previously said, accessible investigations, such as USG and CT scan, are costly, time-consuming, and require more sophisticated tools and training. Some investigations, however, are neither practical nor readily available[63].

The diagnosis of acute appendicitis is supported by the use of a variety of clinical grading systems. A clinical scoring system helps improve the first evaluation. The Alvarado scoring system is the most often used of the several scoring systems that are now available. It is supported by historical research, a physical examination, and a few scientific tests. It is a straightforward, cost-effective addition to the clinical diagnosis of acute appendicitis.

Although the clinical diagnosis is still the mainstay of diagnosing acute appendicitis, their purportedly outstanding results were not always repeatable in everyday situations. Clinical diagnosis might be challenging in cases involving youngsters, the elderly, and females who are close to menarche. Clinical examination precision varied greatly depending on the examiner's experience, ranging from 71 to 97%. Surgeons have always accepted a 20% probability of unsuccessful appendectomy due to the urgent and life-threatening implications of missing a ruptured appendix[65].

The present study was undertaken to evaluate the diagnostic utility of RDW and platelet indices (PDW and MPV) in correlation with the clinical diagnosis of acute appendicitis and in predicting perforation.

TABLE 7: COMPARISION OF GENDER-WISE DISTRIBUTION OF APPENDICITIS CASES WITH OTHER STUDIES

Study	**Number of cases**	**Male: Female ratio**
Boshnak N *et al*[66]	200	1.1:1
D Saxena *et al*[67]	213	2.5:1
Present study	**190**	**1.5:1**

The male-to-female ratio in the present study's appendicitis cases was 1.5:1, which indicates a higher male prevalence. This is comparable to other research that also found that acute appendicitis is more common in men than women[66,67].

TABLE 8: COMPARISON OF MEAN AGE DISTRIBUTION IN ACUTE APPENDICITIS CASES WITH OTHER STUDIES

Study	**Cases**	**Mean age**	**p value**
Boshnak N *et al*[66]	200	29.1±16.3	0.004
Albayrak *et al*[68]	226	32.5±15.1	0.36
Dinc *et al*[69]	295	29.9 ± 12.0	0.930
Present study	**190**	**28.04 ± 14.2**	**0.076**

The age range in the current study was 7 - 72 years. In our study, patients' ages ranged from 28.04± 14.2 years on average. Most of the patients with appendicitis were in their second or third decades of life. This is consistent with prior research.[66,68,69]. No discernible statistical difference between the instances was found. Table 7

HEMATOLOGICAL PARAMETERS

TABLE 9: COMPARISION OF MEAN VALUE, CUTOFF, SENSITIVITY AND SPECIFICITY OF TOTAL LEUCOCYTE COUNT WITH OTHER STUDIES

Parameters			**Studies**		
			Kostakis *et al*[70]	Boshnak N *et al*[66]	**Present study**
TLC/cmm	**Mean value**	**Cases**	14186 ± 4034	**12590±3400**	**12211±5611**
		P value	≤ 0.000	**0.001**	**0.026**
	Cut off		9000	**16100**	**5300**
	AUC (95% CI)		0.96 (0.94-0.99	**0.746 (0.68-0.805)**	**0.649 (0.49-0.809)**
	Sensitivity(%)		**91**	**44.83**	**96.5**
	Specificity (%)		**92**	**100**	**19**

We observed the cut-off value for total count of 5300 with sensitivity 96.5% and specificity being 19%.

Our study shows statistical significance (p-value 0.026) for leukocyte count with the mean value being 12211±5611, which is similar to other studies done as explained in table 9.

PLATELET COUNT

TABLE 10: COMPARISION OF MEAN OF PLATELET COUNT WITH OTHER STUDIES

Study	**Cases**	**Platelet count**	**p value**
Aydogan *et al*[71]	181	328.45±45	0.001
Boshnak N *et al*[66]	145	237.45±54.08	0.02
Present study	**190**	**286 ± 83.5**	**0.44**

In our study we found that statistically there was no difference between the acute appendicitis group and perforated group, which is similar to the results of other studies done by Erdem *et al*[72], Albyarak *et al*[68] and Mehmat *et al*[73]. Thus, our analysis found no association of platelet count variations in acute appendicitis. (Table 9)

In the present study mean platelet count in the acute group was 283±70.19 and the perforated group 311±154 with no significance. (p=0.44)

RED BLOOD CELL DISTRIBUTION WIDTH (RDW)

TABLE 11: COMPARISON OF RDW IN ACUTE APPENDICITIS WITH OTHER STUDIES

Study	**Cases**	**RDW (%)**	**P value**
Narci *et al*[74]	590	15.4±1.5	0.01
Aktimur *et al*[75]	469	12.3±1	0.292
Tanrikulu *et al*[76]	260	13.59±1.24	0.478
Present study	**169**	**14.71±1.64**	**0.442**

TABLE 12: COMPARISION OF CUTOFF, SENSITIVITY AND SPECIFITY OF RDW IN ACUTE APPENDICITIS WITH OTHER STUDIES

Study	**Cut off (%)**	**AUC**	**Sensitivity**	**Specificity**
Narci *et al* [74]	15.6	0.62	47	67
Tanrikulu *et al*[76]	14.5	0.72	18.5	92.4

Present study	**14.15**	**0.449**	**59**	**48**

TABLE 13: COMPARISON OF RDW IN PERFORATED APPENDICITIS WITH OTHER STUDIES

Study	**Cases**	**RDW (%)**	**P value**
Boshnak N *et al*[66]	20	13.30±0.58	NS
Dinc *et al*[67]	117	12.91±1.21	0.285
Present study	**169**	**14.71±1.64**	**0.442**

Note: NS- Not significant p value

The RDW is an automated measurement of the heterogeneity of red blood cell size and is mostly employed in the differential diagnosis of anemia. It is computed by dividing the mean corpuscular volume by the percentage of the red cell volume's standard deviation. A change in RDW level has been observed in a few viral and inflammatory diseases.

Inflammatory mediators have been reported to alter the survival of red blood cells in circulation by inhibiting erythrocyte maturation, which causes newer, larger reticulocytes to enter the peripheral circulation and increases RDW. The RDW in our study was found to be 14.71±1.64, which was not significant with a p-value of 0.442. Similar results were seen in the other studies conducted by Aktimur *et al*[75] and Tanrikulu *et al*[76].

However, it was noted that RDW was elevated in the perforated group when compared to the acute group, similar to the study by Boshnak N *et al*[66], which shows the high-grade inflammatory pathology of perforated appendicitis, thus can be used as a predictive indicator.

PLATELET INDICES:

Platelet indices (MPV and PDW) were analyzed in acute appendicitis cases and compared with age and sex-matched.

MEAN PLATELET VOLUME

The MPV value evaluated in our study was 9.27 ± 1.06 fl in the acute appendicitis group and 8.47±1.26 fl in the perforated group. We found that MPV is significant (p-value 0.002) in acute appendicitis patients when compared with the perforated group.

TABLE 14: COMPARISON OF MPV IN ACUTE APPENDICITIS WITH OTHER STUDIES

Study	**Cases**	**MPV (fl)**	**p-value**
Narci *et al*[74]	590	7.92±1.68	<0.001
Erdem *et al* [72]	100	7.4±0.9	<0.001
Aktimur *et al*[75]	469	9.6±1.5	0.018
Tanrikulu *et al*[76]	260	7.75±1.24	0.001
Present study	**169**	**9.27 ± 1.06**	**0.002**

TABLE 15: COMPARISION OF CUTOFF, SENSITIVITY AND SPECIFICITY OF MPV IN ACUTE APPENDICITIS WITH OTHER STUDIES

Study	**Cut off (fl)**	**AUC**	**Sensitivity**	**Specificity**
Narci *et al*[74]	7.87	0.62	66	59
Erdem *et al*[72]	7.95	0.824	74	75
Aktimur *et al*[75]	9.6	0.595	57.1	60.7
Tanrikulu *et al*[76]	7.3	0.79	45	89.2
Present study	**9.05**	**0.711**	**57**	**81**

TABLE 16: COMPARISON OF MPV IN PERFORATED APPENDICITIS WITH OTHER STUDIES

Study	**Cases**	**MPV (fl)**	**p-value**
Aydogan *et al*[71]	21	12.51±0.55	0.0001
Dinc *et al*[67]	117	8.26±1.06	0.767
Boshnak N *et al*[66]	20	11.14±0.75	NS
Present study	**21**	**8.47± 1.26**	**0.002**

Note: NS- p value not significant

A decrease in MPV is thought to result from increased sequestration and destruction of activated platelets at the inflammation site, whereas an increase in MPV is thought to result from early platelet activation brought on by inflammation and a late increase in the release of young platelets into circulation from the bone marrow.

Variations in MPV may be indicative of inflammation, according to numerous research on non-infectious inflammatory diseases. Studies on acute appendicitis and the function of MPV in its diagnosis have revealed that variations in MPV values, such as higher or lower levels, are acceptable.

Although, in our study MPV was found to be statistically significant (p-value 0.002). Also, there was a decrease in MPV in the perorated group compared to the acute group. which was in concordance with studies conducted by Erdem *et al*[72] and Tanrikulu *et al*[76], thus establishing MPV association in acute appendicitis and predicting perforation.

We got a cut-off of 9.05fl (p-value 0.002*) for which sensitivity was 57% and specificity was 81% the results were comparable to Aktimur *et al*[75] study results as mentioned in the above table (Table 15)

PLATELET DISTRIBUTION WIDTH:

To our knowledge, only few studies have investigated the changes in PDW values in acute appendicitis.

TABLE 17: COMPARISON OF PLATELET DISTRIBUTION WIDTH (PDW) IN ACUTE APPENDICITIS WITH OTHER STUDIES

Publication	**Cases**	**PDW (fl)**	***p* value**
Dinc *et al*[67]	295	49.0 (10.6-86.5)	<0.001
Boshnak N *et al*[66]	145	14.25±2.10	<0.001
Madani *et al*[73]	39	11.9 (11.2-13.6)	NS
Present study	**169**	**11.6±1.91**	**0.036**

Note: NS- p value not significant

TABLE 18: COMPARISION OF CUTOFF, SENSITIVITY AND SPECIFICITY OF PDW IN ACUTE APPENDICITIS WITH OTHER STUDIES

Study	**Cut off (fl)**	**AUC (95% CI)**	**Sensitivity**	**Specificity**
Dinc *et al*[67]	32.15	0.95	97.1	93
Boshnak *et al*[66]	14.2	0.646	48.28	90.91
Present study	**10.45**	**0.641**	**73**	**62**

TABLE 19: COMPARISON OF PLATELET DISTRIBUTION WIDTH (PDW) IN PERFORATED APPENDICITIS WITH OTHER STUDIES

Publication	**Cases**	**PDW (fl)**	***p* value**
Boshnak N *et al*[66]	20	12.85±0.96	0.002
Present study	**21**	**10.92±2.47**	**0.036**

The quantity of platelets changes during an acute inflammatory process, causing bigger platelets to enter the circulation and, as a result, a spike in subsequent PDW levels. Young platelets are entering the peripheral circulation when MPV and PDW are higher than controls. MPV and PDW are both platelet immaturity markers.

Our evaluation showed that PDW is statistically significant with p value= 0.036 in the patients of acute appendicitis (11.6±1.91 fl) as compared to the perforated group (10.92±2.47 fl). Similar results were noted in other studies as compared in table. However, the PDW value was decreased in the perforated group compared to the acute group, which is suggestive of high-grade inflammation. Hence, a decrease in PDW can be used as a prognostic indicator of disease activity in perforated appendicitis. (Table16)

In our study, we got a cut-off of 10.45fl for PDW, for which sensitivity was 73% and specificity was 62%. This was comparable with the other studies mentioned in the table number 18.

CONCLUSION

- Platelet indices and RDW along with leucocytosis play an important role in the diagnosis of acute appendicitis and perforated appendicitis and can be used in predicting it preoperatively.
- We found MPV and PDW showed statistically significance in both acute and perforated appendicitis, also MPV and PDW were observed to be decreased in perforated appendicitis, which indicates the high-grade inflammation, thus can be used as predictive markers.
- RDW showed no significance among the both groups, however the perforated appendicitis showed higher RDW compared to acute appendicitis.
- Thus, the value of these can be used as added diagnostic and predictive markers of appendicitis, which are readily available in basic routine complete blood count test with no added socio-economic burden to the patients.

SUMMARY

- The study titled 'Evaluation of Platelet Indices And Red Cell Distribution Width As Emerging-Biomarker For The Diagnosis Of Acute Appendicitis And Appendicular Perforation' was undertaken in B.L.D.E. (Deemed to be University) Shri B. M. Patil Medical College, Hospital and Research centre, Vijayapura,
- Total of 190 patients were part of the study of which 169 were acute appendicitis and 21 perforated appendicitis confirmed histopathologically, whom were evaluated for RDW, MPV and PDW in establishing relationship for diagnosis of acute appendicitis and its complication.
- Majority of the patients with appendicitis belonged to 2^{nd} and 3^{rd} generation with male predominance of M: F=1.5:1.
- Our study shows statistical significance (p-value 0.026) for leukocyte count with the mean value being 12211±5611, with cut-off value of 5300 with sensitivity 96.5% and specificity being 19%.
- RDW in our study was found to be 14.71±1.64, which was not significant with a p-value of 0.442. However, it was noted that RDW was elevated in the perforated group when compared to the acute group.
- MPV was found to be statistically significant (p-value 0.002), with cut-off of 9.05fl (p-value 0.002) for which sensitivity was 57% and specificity was 81%.
- PDW is statistically significant with p value= 0.036 in the patients of acute appendicitis (11.6±1.91 fl) as compared to the perforated group (10.92±2.47 fl), with cut-off of 10.45 fl for PDW, for which sensitivity was 73% and specificity was 62%.
- Thus, the severity of perforation appendicitis is indicated by the decreased MPV and PDW value along with raised RDW, hence these can used as additional diagnostic markers in diagnosis and predicting appendicitis.

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ANNEXURE II

SAMPLE INFORMED CONSENT FORM

B.L.D.E.U.(DU) SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA – 586103, KARNATAKA

TITLE OF THE PROJECT **EVALUATION OF PLATELET INDICES AND RED CELL DISTRIBUTION WIDTH AS EMERGING-BIOMARKER FOR THE DIAGNOSIS OF ACUTE APPENDICITIS AND APPENDICULAR PERFORATION**

.

PRINCIPAL INVESTIGATOR: **Dr. CHETAN.A.G**
DEPARTMENT OF GENERAL SURGERY.

PG GUIDE: **Dr. VIJAYA L. PATIL**
M.S. (GENERAL SURGERY)
PROFESSOR, DEPARTMENT OF GENERAL SURGERY

PURPOSE OF RESEARCH:

I have been informed that this study will analyse the usefulness of platelet indices (MPV

and PDW) and RDW in diagnosis of acute appendicitis and its complications.

I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

PROCEDURE:

I understand that relevant history will be taken. I will do detailed clinical examination after which necessary investigations will be done whenever required, which would help the investigator for appropriate management.

RISKS AND DISCOMFORTS:

I understand that my ward may experience some pain and discomfort during the examination or during my treatment. This study is not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that I/my wards participation in this study will help in early, feasible, and routinely done investigation to diagnose acute appendicitis.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr. CHETAN.A.G is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. CHETAN.A.G will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to_____the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date: Dr. VIJAYA L PATIL Dr. CHETAN.A.G

(Guide) (Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. CHETAN.A.G has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own understandable language.

I have been explained all the above in detail in my own language and I understand the same. Hence, I agree to give my consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

ANNEXURE III

PROFORMA:

CASE NO:

- Name: IP No:
- Age/sex: DOA:
- Occupation: DOD:
- Address:

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

PAST HISTORY:

PERSONAL HISTORY:

- Diet
- Sleep
- Appetite
- Bowel & bladder

GENERAL PHYSICAL EXAMINATION:

- Mental Status
- Built
- Nourishment
- Pallor
- Icterus
- Cyanosis
- Clubbing
- Edema
- Cervical Lymph Nodes

- Pulse
- Blood pressure
- Temperature
- Respiratory rate

SYSTEMIC EXAMINATION

PER ABDOMEN*:*

Inspection:

Palpation:

Percussion:

Auscultation:

RERSPRATORY SYSTEM:

CARDIO-VASCULAR SYSTEM*:*

CENTRAL NERVOUS SYSTEM*:*

DIAGNOSIS

B.L.D.E. (DEEMED TO BE UNIVERSITY) IEC/NO-09/2021 Date-22/01/2021

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis

Name of PG student: Dr Chetan A G, Department of Surgery

Name of Guide/Co-investigator: Dr Vijaya.L. Patil, Professor
Department of Surgery

DR .S.V.PATIL
CHAIRMAN, IEC

Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

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KEY TO MASTER CHART

M	**Male**
F	**Female**
TLC	**Total Leucocyte Count**
PLT	**Platelet Count**
RDW	**Red Blood Cell Distribution Width**
MPV	**Mean Platelet Volume**
PDW	**Platelet Distribution width**
HPR	**Histopathology report**
AA	**Acute Appendicitis**
PA	**Perforated Appendicitis**

MASTERCHART

Sl No	IP No	Name	Age	Sex	TLC	PLT	PDW	MPV	RDW	HPR
1	23995	Jyothi	38	Female	6740	269	12.7	11.2	15.3	AA
2	25546	Nilesh	10	Male	12010	311	10.9	10.1	13.4	AA
3	25588	Babu	27	Male	4940	90	12	10.8	12.3	AA
4	26703	Manikawa	10	Female	8770	150	13.8	11.2	14.8	AA
5	26636	Nikil	22	Male	7730	281	11.1	8	14	AA
6	37095	Lalithabai	60	Female	11030	228	14	9.2	16.4	AA
7	42035	Yallawa	44	Female	5830	202	10.2	10.4	13.2	AA
8	51947	Kashibai	55	Female	14970	349	11.4	10.2	12.8	AA
9	52162	Rameja	45	Female	10160	478	10.2	10	18	AA
10	52809	Savithri	30	Female	7100	303	9.4	9	14.2	AA
11	55640	Prakesh	58	Male	15870	367	10	9	21.9	AA
12	59328	Gururaj	28	Male	9020	333	9.9	10	13.5	AA
13	59638	Kiran	27	Male	8720	160	17.1	9.2	15.5	AA
14	61256	Abdul	30	Male	20780	339	9.9	9.2	18.4	AA
15	63031	Sunanda	57	Female	18600	502	8.7	8.2	14.5	AA
16	64654	Nithin	25	Male	20390	184	9.6	9.4	13.1	AA
17	67842	Shreedevi	28	Female	9690	317	11.6	10.3	12.1	AA
18	68039	Kamalabai	37	Female	8200	312	8.6	8.6	12.6	AA
19	82173	Anand	22	Male	8680	280	12	10	14.7	AA
20	85719	Ramagouda	21	Male	13710	229	10.9	9.8	14.7	AA
21	87312	Balawwa	63	Female	22870	224	15.2	11.7	16.7	AA
22	90539	Savithri	20	Female	9870	278	11.9	10.4	15.3	AA
23	96136	Akash	16	Male	6550	356	9.7	9.2	14	AA
24	96635	Raju	20	Male	10710	272	11.1	10.3	20.3	AA
25	118105	Bhagyashree	12	Female	8060	285	18	10	15.3	AA
26	116103	Vaishali	23	Female	10200	271	13.2	10.8	12.7	AA
27	124117	Raju	23	Male	21260	71	13.3	9.3	13.7	PA
28	145701	Karuna	21	Male	11440	315	8.8	8.9	14.9	AA
29	150777	Shreshail	22	Male	8930	383	9.7	7.5	15.1	AA
30	161532	Ajay	21	Male	4450	291	9.3	7.6	13.3	AA
31	164172	Aslam	11	Male	15030	374	13.9	8.8	13.9	AA
32	167747	Sumitra	27	Female	6700	265	11.8	8.4	12.9	AA
33	170038	Bhagyashree	12	Female	7410	420	9.6	9.2	13.6	AA
34	168219	Vidyashree	18	Female	29800	363	10.4	8	16.7	AA
35	6024	Deeksha	21	Female	12460	395	10.1	9.8	15.2	AA
36	4533	Chetan	16	Male	8960	315	13.1	8.6	15.8	AA
37	3562	Mahadevi	28	Female	5360	320	11.4	8.1	15.7	AA
38	22390	Bsavaraj	32	Male	6240	269	11.7	8.4	15.4	AA
39	57827	Spoorthi	7	Female	7940	424	10.5	9.2	20	AA
40	97486	Sumitra	25	Female	5050	137	11.2	10.8	16.2	AA
41	66135	Mallappa	45	Male	8380	403	11.3	10	12.6	AA
42	83756	Jagadish	37	Male	8140	251	11.5	9.6	15.9	AA
43	73756	Mallu	20	Male	8390	237	15.2	9.5	16.3	AA
44	51290	Ajit	13	Male	10580	176	14	9.6	14.3	AA
45	152672	Mudakanna	35	Male	23810	496	10.4	7.5	13.4	PA
46	89656	Sangappa	25	Male	5860	262	11.4	8.2	13.8	AA
47	83463	Preranna	16	Female	13390	377	9.8	7.5	14	PA
48	166923	Mukthar	54	Male	11870	198	15.2	9.4	13.2	AA

49	168740	Monika	17	Male	11280	242	13.9	8.8	22.4	PA
50	168608	Vivek	22	Male	7540	322	12.2	8.2	14.1	AA
51	185695	Swetha	18	Female	611	156	12.4	9	20.1	PA
52	191370	Siddu	13	Male	7470	441	12.1	8.2	13.1	AA
53	192538	Harish	17	Male	14930	338	11.3	8	15.1	AA
54	198625	Pruthvi	6	Male	19630	333	12.5	8.3	13	AA
55	201219	Deepali	25	Female	12740	285	13.3	11.2	12.8	AA
56	204062	Rakshita	10	Female	10470	259	11.5	10.2	12.9	AA
57	217072	Soundarya	17	Female	8580	233	10.4	9.6	13.9	AA
58	223993	Arvind	37	Male	7310	241	13.1	8.5	13.7	AA
59	225398	Aruna	40	Female	11690	249	9.1	7.1	16.3	AA
60	226382	Bhimaya	42	Male	13450	362	9.8	7.2	14	AA
61	230851	Suresh	48	Male	11300	331	13.2	8.8	16	AA
62	241164	Vedantha	13	Male	8530	330	12.2	8.3	14.9	AA
63	248562	Rajashekar	27	Male	10100	287	18.3	11.1	15.7	AA
64	254812	Jakhar	27	Male	10500	395	10.2	7.4	14.2	AA
65	259631	Subramya	17	Male	16680	319	9.7	7.4	15.6	AA
66	264951	Nigamma	36	Female	6400	231	14.7	9.3	14.7	AA
67	272347	Shivarudrappa	17	Male	12900	306	15.3	9.6	16.9	AA
68	276438	Preetam	12	Male	10560	329	11.4	7.8	15.6	AA
69	134320	Poonam	17	Female	10400	338	8	8.1	14	PA
70	290739	Ragavendra	35	Male	11270	333	13.9	9	13	AA
71	291183	Kavita	27	Female	10490	398	17.4	8.9	20	PA
72	293066	Kaveri	17	Female	10980	299	9.9	9	12.3	AA
73	292036	Basavaraj	28	Male	6540	225	14.6	9.5	14.5	AA
74	310447	Akshata	26	Female	9440	343	10.4	7.9	15.3	AA
75	312640	Shruthi	14	Female	10720	321	13.9	9	14.1	AA
76	20	Sunil	25	Male	12790	209	11.7	8.2	15.2	AA
77	1313	Mangla	34	Female	16170	295	11.3	7.8	16.2	AA
78	8827	Mallangouda	31	Male	4210	230	15.6	10.7	19.5	PA
79	11486	Prasad	14	Male	20580	302	10.7	7.9	13.2	AA
80	19956	Santosh	29	Male	7720	315	10.6	7.5	14.4	AA
81	32943	Pavitra	21	Female	10360	368	9.7	7.2	16.1	AA
82	26798	Sanjana	13	Female	5920	171	10.7	8	15.5	AA
83	38320	Siddaray	25	Male	4500	171	11.2	8.4	15.1	AA
84	39731	Somanth	21	Male	11050	360	12.6	8.7	15.3	AA
85	39936	Bhagyashree	9	Female	4850	302	13.1	8.3	16.5	AA
86	40800	Shankaray	23	Male	27700	675	9.3	7.2	14.6	PA
87	45556	Mahadevappa	16	Male	7350	226	15.9	10.1	15.6	AA
88	49436	Dattu	35	Male	6960	170	11.6	8.5	15.5	AA
89	50627	Choupanbee	34	Female	18750	429	11.9	8.2	14.8	PA
90	53945	Sharukhan	23	Male	10110	235	12.7	8.6	14.2	AA
91	55884	Areeba	23	Female	12710	267	12.5	8.7	14.6	AA
92	58790	Sangappa	69	Male	5040	402	9.5	7.2	16.5	PA
93	63664	Jyothi	13	Female	14610	231	13.4	8.6	14.8	AA
94	63769	Sarubai	45	Female	5240	444	10.1	7.5	18.6	PA
95	66088	Shilpa	25	Female	9380	325	14	8.8	13.9	AA
96	83163	Ambika	40	Female	7560	276	13	9	14.2	AA
97	84526	Karan	18	Male	10100	292	13.9	9	14.9	AA
98	91694	Prakash	30	Male	6900	264	14.9	9.2	14.9	AA
99	91764	Ashwini	18	Female	11170	287	10.9	7.9	16.2	AA
100	91530	Muskani	18	Female	8560	366	14.2	8.7	17.6	AA
101	94837	Somanraj	24	Male	10010	192	15.8	9.8	13.6	AA

102	96031	Bandavva	35	Female	9880	263	10.2	7.6	16.4	AA
103	82683	Bouramma	60	Female	8910	332	10.8	7.6	15.2	AA
104	98277	Anasab	60	Male	9800	226	14.5	9.2	14.2	AA
105	98945	Renuka	30	Female	11100	265	11.4	8.2	13.8	AA
106	98918	Shrishail	20	Male	18740	360	11.6	8.1	13.5	AA
107	2549	Manjunath	31	Male	13950	350	14.8	9.3	16.4	AA
108	294154	Laxmi	26	Female	9380	277	10.4	7.5	16.6	AA
109	103477	Iranna	10	Male	14200	438	9.1	7.2	15.8	PA
110	104881	Parvathi	50	Male	8920	409	11.5	7.9	14.2	AA
111	107553	Pooja	18	Female	7990	236	13.9	8.9	13.7	AA
112	111875	Mallikarjun	50	Male	6540	202	13	8.5	14.3	AA
113	117188	Santosh	30	Male	6710	310	10.5	7.7	16.9	AA
114	117593	Malappa	36	Male	11860	346	17	9.2	17.9	AA
115	124111	Savitha	24	Female	14920	326	1535	9.5	14.5	AA
116	125545	Ashok	25	Female	6970	368	12.1	8.4	14	AA
117	127135	Abhishek	22	Male	16730	298	10.4	7.8	13.6	PA
118	128865	Omkar	20	Male	7980	411	9.2	7.1	14.4	AA
119	130586	Vinod	10	Male	8360	454	8.2	7	14	PA
120	134341	Mallanna	21	Male	11270	244	10.3	7.7	13.5	AA
121	138021	Shivanna	40	Male	9440	262	10.9	7.9	16.8	AA
122	157548	Manjula	35	Female	9820	310	11.3	7.8	14.9	PA
123	12396	Samarth	15	Male	15310	368	9.4	8.9	12.6	AA
124	142468	Gundappa	34	Male	10010	197	12.2	8.5	15.3	AA
125	144368	Bharathi	30	Female	8040	205	13.4	8.6	16.2	AA
126	151656	Amasidda	50	Male	12970	216	10.8	8.1	15	AA
127	159636	Namitha	10	Female	10210	178	11.1	9.9	12.4	AA
128	161452	Revanasidda	36	Male	9300	287	10	9.3	13	AA
129	154922	Prubuling	19	Male	11630	256	10	9.2	16.7	AA
130	164295	Bhayakka	50	Female	10630	296	10	9.8	14.7	AA
131	168727	Basanna	70	Male	13360	199	10.5	10.6	14.3	AA
132	84566	Neeraj	24	Male	9610	286	12.2	10.8	14.3	AA
133	177426	Parushram	18	Male	8100	302	9.5	8.7	11.8	AA
134	179064	Akshata	15	Female	9660	369	8.7	9	16.6	AA
135	179383	Sandeep	10	Male	12010	256	9	8.4	17	AA
136	181639	Girija	26	Female	6840	215	10.6	9.6	12.8	AA
137	184588	Ashwini	22	Female	13200	269	8.8	10	15	AA
138	187528	Ramesh	78	Male	20090	224	12	11.2	14.1	PA
139	189088	Vithal	26	Male	8120	305	11.1	10.1	13.9	AA
140	189389	Bhagwatray	16	Male	15630	412	10.7	9.9	13.8	AA
141	190654	Karthik	15	Male	8140	308	10	9.1	14.2	AA
142	189071	Anil	23	Male	6940	239	10.8	10.2	14.6	AA
143	191827	Akshata	12	Female	15590	331	8.9	9.4	15.2	AA
144	192514	Runuka	38	Female	8120	477	11	9.9	18.2	AA
145	196759	Ramachandra	11	Male	5640	234	8.6	8.2	14.5	AA
146	197893	Ayyappa	15	Male	15850	331	9.9	9.6	15.3	AA
147	199757	Bhimshankar	18	Male	15910	230	10.9	9.8	12.7	AA
148	192695	Chanhbasha	38	Male	6670	229	11.7	9.9	13.3	AA
149	158683	Vidya	30	Female	9740	288	10.9	9.8	14	AA
150	175798	Shashikala	25	Female	10410	292	11.1	10.4	14.9	AA
151	209291	Santosh	30	Male	7430	167	14.6	11.1	14.9	AA
152	196739	Rashikala	33	Female	12350	365	9.6	10.2	16.8	AA
153	211961	Manjula	37	Female	13800	298	10.5	11	17	AA
154	213251	Sagar	24	Male	10300	230	11.3	10.8	19.3	AA

155	24451	Arun	19	Male	9620	213	10.7	11	14.5	AA
156	28630	Yallappa	33	Male	12030	265	11.6	9.9	13.8	AA
157	28636	Vivekanand	32	Male	11000	214	10.8	11.3	13.4	AA
158	32104	Anand	33	Male	8560	221	10.3	10.1	12.2	AA
159	40454	Ramesh	28	Male	13600	281	11.3	10.8	14.6	AA
160	40800	Shivappa	70	Male	9620	345	10.7	9.8	15.6	AA
161	47286	Saman	15	Male	6530	312	11.6	10	14.1	AA
162	47286	Vikas	19	Male	10230	265	10.6	9.7	13.2	AA
163	64091	Jayashwar	10	Male	9650	296	11.6	11	12.5	AA
164	70820	Bhimshankar	21	Male	8620	230	10.5	10.9	13.7	AA
165	64865	Roopa	27	Female	10300	302	10.2	11.3	15.2	AA
166	99548	Gitabai	30	Female	8620	254	11.3	9.7	13	AA
167	105877	Siddiq	11	Male	11350	223	12	10.2	14.2	AA
168	13790	Vidya	30	Female	16000	214	11.1	10.2	13.9	AA
169	111281	Sampath	12	Male	10020	210	10.9	10.2	14.2	AA
170	252995	Nagesh	26	Male	14500	265	10.9	11.2	16.7	AA
171	217280	Jeetu	30	Male	18900	168	9.2	8.6	15.3	PA
172	286772	Maruthi	36	Male	10230	212	10.6	9.2	14.8	AA
173	205975	Baiyappa	39	Male	19300	112	9.1	8.5	12.9	PA
174	215045	Bhimabai	60	Female	12300	265	10.6	9.5	13.8	AA
175	215354	Sangeeta	32	Female	12600	210	10.6	10.1	14.2	AA
176	213897	Ramesh	26	Male	6000	218	10.4	9.7	13.9	AA
177	217287	Nilakka	21	Female	5170	220	11.3	9.8	13.5	AA
178	224275	Rajashekar	28	Male	8020	270	10.5	9.2	14	AA
179	225886	Mansur	16	Male	6520	350	10.5	9.6	13.6	AA
180	227011	Mutanna	58	Male	9450	148	9.2	8.8	12.8	PA
181	234261	Vaishali	22	Female	8460	297	11.3	9.8	13.6	AA
182	239613	Paranawwa	32	Male	8350	326	13.7	11.1	17.7	AA
183	241863	Gurushanth	61	Male	23860	128	9.4	11.2	12.9	PA
184	243959	Channagouda	26	Male	12530	268	12.2	9.9	12.9	AA
185	242980	Gurappa	60	Male	7840	334	9.6	8.4	12.9	AA
186	252241	Sangamesh	55	Male	11820	171	13.9	10	12.1	AA
187	252249	Hitesh	24	Male	9610	277	13	10.1	13.6	AA
188	253852	Shankaring	40	Male	13370	240	9.2	8.9	13.3	AA
189	258426	Shruthi	12	Female	20620	168	11.7	10.3	13.2	AA
190	259075	Archana	24	Female	7530	316	10.5	10	13.9	AA