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College of Veterinary Medicine

A Comparative Study between Aloe Vera gel and Platelet Rich Fibrin in Hernioplasty of Surgically Induced Abdominal Hernia in Rams

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By

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الاية

بسم الله الرحمن الرحيم

﴿ فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ ۗ وَلَا تَعْجَلْ بِالْقُرْآنِ مِن قَبْلِ أَن يُقْضَىٰ إِلَيْكَ وَحْيُهُ ۖ وَقُل رَّبِّ زِدْنِي عِلْمًا ﴾

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I certify that this dissertation entitled " **A Comparative Study between Aloe Vera gel and Platelet Rich Fibrin in Hernioplasty of Surgically Induced Abdominal Hernia in Rams "was** prepared under my supervision at the College of Veterinary Medicine / University of Mosul, as a partial fulfillment of the requirements for the degree of Ph.D. in Veterinary surgery.

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Ibrahim

Abstract

The study was designed to assess the healing process for repairing of experimentally induced major abdominal wall hernias using polypropylene (PP) mesh alone or enhanced with Aloe Vera gel or PP mesh enhanced with platelets rich fibrin (PRF). Thirty six adult rams were used that randomly divided into three groups, one control and two treated groups, twelve animals for each one. Under protocol of deep sedation and local anesthesia, the site of operation was prepared aseptically, 10cm diameter of ventrolateral abdominal wall hernias were created, then left for one month later, and then hernioplasty was done according to the following:

- Group 1: (control) repaired with modified sublay implantation of PP mesh
- Group 2: repaired with modified sublay implantation of PP mesh with prepared Aloe Vera gel.
- Group 3: repaired with modified sublay implantation of PP mesh with PRF.

In this, work healing process and abdominal wall restoration at the site of induced hernia were monitored along 45day trial by clinical, ultrasonographical, laparoscopic, microscopical, and immunohistochemically, investigations. In all experimental animals, clinical evaluations of the hernia after its induction, reconstruction, and repair showed unspecified secondary health problems. While ultrasound examination on days 7, 15, 30, and 45 after surgery showed that the hernia signs gradually diminished at the end of study while laparoscopic investigations indicated complete adhesion of the omentum with implanted polypropylene mesh and edges of abdominal wall at the hernia area. The stability of adhesion increased with the times, and there were no intestinal or other internal organ adhesions furthermore the histopathological assessment indicated there was early healing process in G3 which represented by presence a high number of new blood vessels with deposition of collagen fibers whereas immunohistochemistry investigations of IL-6 in both control and PRF group

indicated a strong positive reaction on days 7 to 15 post-hernioplasty that appeared as golden-brown granules in the cytoplasm of cells around the surgical mesh, but in PRF group on day 30 post-surgery it was indicated a weak positive reaction in few cells with IL-6 antibody IHC. Besides immunohistochemistry expression for VEGF in Aloe Vera group on day 7 indicated negative reaction, while on day 15 to day 45 post-surgery indicated positive reaction with vascular endothelial growth factor (VEGF) that appeared as golden-brown granules in cytoplasm of cells around surgical mesh.

The results of scoring analyzed inflammatory reaction indicated different response between highest inflammatory reaction that appear in the control group followed by Aloe Vera group and highest rate showed in PRF group. In the PRF group the amount of granulation tissue formation was lowest

Angiogenesis and subsequent newly blood vessels were presence and increased along the period of post-surgery especially in PRF, but the number of newly blood vessels formation decreased on day 45 especially in PRF followed by Aloe Vera group and there was significant differences between the different groups at $P<0.05$.

The fibrous tissue deposition noticeable increased from day 7 to day 30 post operation especially in PRF group as compare to other group. On other side after day 45 post-surgery the amount of fibrous tissue deposition decreased dramatically in PRF group as compare to other groups, this action occurs as soon as these collagen fibers stretched and mature.

In conclusion, using PRF to repaired hernia reduces the incidence of post-operative pain, inflammation, and histopathological and immunohistochemistry investigations emphasize an promoting healing process of hernia and facilitating the formation of new blood vessels and cytokines, beside using Aloe Vera gel, prevent infection and abscess formation and enhanced healing.

Contents

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List of Abbreviations

PP	polypropylene mesh
PRF	platelet rich fibrin
L-PRF	Leukocyte- and platelet-rich fibrin
PRP	platelet rich plasma
US	Ultrasonography
CT	computed tomography
MRI	magnetic resonance imaging
IPOM	intraperitoneal onlay mesh
TAPP	transabdominal preperitoneal
TEP	totally extraperitoneal
VH	ventral hernias
CA	cyanoacrylates
PET	polyester
LVHR	laparoscopic ventral hernia repair
ePTFE	expanded polytetrafluoroethylene
MSCs	mesenchymal stem cells
GFs	growth factors
CTGF	connective tissue growth factor
BMP-2	bone morphogenetic protein 2
TGF	transforming growth factor
IGF-I	insulin-like growth factor
PDGF	platelet-derived growth factor
PPP	platelet-poor plasma
ECM	extracellular matrix
HSPs	heat shock proteins
PMNs	polymorphonucleocytes

ILs	Interleukins
FGF	Fibroblast growth factor
VEGF	Vascular endothelial growth factor
MSCs	Mesenchymal stem cells
TGF β-1	Transforming growth factor beta 1
VLUs	venous leg ulcers
PUs	pressure ulcers
DFUs	diabetic foot ulcers
C3a and C5a	chemotactic factors for inflammatory cells
IHC	Immunohistochemistry
HIF	hypoxia-induced factor
FBR	foreign body reaction
EGF	Dermatologic growth factor
MMPs	matrix metallo-proteinases

Chapter One

Introduction

Hernial repair is one of the most common operation of surgical correction which performed for abdominal defect around the world. Despite tremendous improvements, implant design still remains a crucial challenge for the successful repair and prevention of recurrent hernias, although there is no perfect mesh for every procedure. The clinical challenge for surgeons is the surgical reconstitution of significant abdominal wall muscle defects, such as ventral hernia. These defects have typically been brought on by trauma or weak abdominal muscles (Haidar, *et al*., 2023). Tight suturing to approximate and close the defect runs the risk of causing wound dehiscence, recurrent hernias, and wounds which fail to heal (Subburaaj, 2023) When the hernial ring size exceeds 3 cm in diameter, prosthetic material must be used during the hernioplasty procedure (Mitura, *et al*,. 2021).The most common reconstructive technique that have been developed, involves the use of non-absorbable synthetic mesh to close abdominal wall defects without tension (Chen, *et al*., 2023). Complications such as mesh extrusion, bowel adhesion, fistula formation, wound infection, skin erosiveness, and seroma development have been associated with use of such non-absorbable synthetic mesh material (Morales-Conde, *et al*,. 2022).

Surgical mesh made of polypropylene (PP) has garnered a lot of interest because of its superior mechanical qualities and chemical inertness. Yet, it needs to be improved to increase biocompatibility and prevent unwanted tissue attachment, and with minimum incidence of tissue rejection, recent mesh innovations include protein anti-adsorption, cellular adhesion, biocompatibility, and anti-microbial resistance of polypropylene (PP) mesh, as well as modification approaches and their evaluations. The prognosis for future developments (Saha *et al*., 2022).

Many studies were used different techniques and materials for reconstitution of the large abdominal wall muscle defect. Such as using Bovine tunica vaginalis in repairing of hernia (Abass, 2008), acellular urinary bladder matrix as a compare with acellular bovine pericardium matrix for reconstitution the large hernia (Al-ebadi, and AL-byaty, 2019).

Many biological materials commonly used for medicinal purposes in many countries as Aloe Vera it contain many inorganic compounds ,vitamins ,enzymes and amino acid which are essential for enhancement of healing, in general this substance is regarded as safe agent when applied topically. It stimulates the ability of hydrocortisone to minimize swelling (Bhuvana, *et al.*, 2014). Aloe Vera properties include antimicrobial immunomodulatory and anti-inflammatory activities because it contains of polysaccharides, essential amino acids and vitamins C that enhance and improve cell regeneration and stimulate the growth of tissues (Azevedo, *et al*., 2019).

The using of platelets rich fibrin PRF with grafting agent is considered as a regenerative agent, that is important in enhancing the healing process in soft tissue (Moheb, *et al.*, 2017) PRP was used with good outcome in combination with mesh for repairing inguinal hernias as a safe and beneficial option for an improving healing process (Valerio and Giovanni 2021).

Due to the absence of studies for using of Aloe Vera leaf gel or (PRF) to enhance the PP mesh, the aim of the current study to compare between the efficacy of Aloe Vera leaf gel and PRF for enhancement of PP mesh properties for reconstitution of large ventro-lateral abdominal wall hernia in Rams .

Chapter Two

Literatures Review

2-1 Anatomy of abdominal wall in sheep

Generally the abdominal wall formed by groups of muscle connected with several structures as fat, fascia, aponeurosis and lastly skin

2-1-1 The tunica flava of abdomen

It is the strong development of the deep fascia of the abdominal wall over the external abdominal oblique muscle and it is aponeurosis (Mansour, *et al*., 2023). It is continuous with the deep fascia of other regions and ventrally its better developed than dorsally it formed by a large number of elastic fibers and a variable amount of fat, It's attached to the linea alba by the mid-ventral line, deeply it is difficult to separate from the external oblique aponeurosis and assists in the formation of the external opening of the inguinal canal. Laterally, easy separated from the underlying structure. It forms the medial the deep fascia of the prepuce and the tunica dartos of the scrotum of ram. The function of the tunic is to assist the abdominal muscles, especially the rectus abdominis, in loading the heavy weight of the internal viscera (May, 1970; Bittner, 2017).

2-1-2 External oblique abdominal muscle

The most superficial muscle of the abdominal wall and covered by the yellowish white, deep facial layer. This muscle originated from the costal wall at the ventral part of the fifth rib slightly dorsal to the middle of the last rib and from the lumbo-dorsal fascia near the ends of the transverse processes of the lumbar vertebrae. The costal origin is by digitations, the more cranial alternating with those

of the ventral serrate muscle, the fibers of muscle directed longitudinally at the upper flank, this do not reach the lumber transverse processes or the tuber coxae. This Aponeurosis blends with the aponeurosis of the internal abdominal oblique muscle. Between the tuber coxae and the prepubic tendon, the caudal edge of the aponeuros of the external abdominal oblique muscle is the thickened to form the inguinal ligament and lies in relation to the ventral edge of the iliacus muscle (konig *et al*., 2007). Superficial branches of the ventral branches of last thoracic and first tow lumber nerves penetrate the muscle along a line from the ventral end of the last rib to the tuber coxae and ramify in the cutaneous muscle and skin. They are accompanied by branches of the lumber arteries .Immediately ventral to the tuber coxae, branches of the anterior branch of the deep circumflex iliac artery can be seen passing cranio-ventral. Action of this muscle is to support and retain the abdominal viscera in position, assist in compressing the abdominal viscera in forced expiration, defecation, micturition, parturition, and coughing and acting singly to produce lateral flexion of the back and assist in arching back (Dyce *et al.*, 2009).

2-1-3 internal oblique abdominal muscle

The muscle fibers originated from lumber fascia, thigh fascia and tuber coxae and inserted by an aponeurosis in to last three or four ribs along the costal arch and to the linea Alba. This fiber directed cranio-ventrally becoming transverse at the dorsal edge. The attachment is dorsally to the lumbo-dorsal fascia, the tuber coxae, and the adjacent part of the inguinal ligament. Ventrally, the aponeurosis blends with that of the external abdominal oblique muscle near the linea Alba (Cavalli *et al*., 2020). At the lowest and caudal point of its fibers, it form the cranial boundary of the external inguinal ring. The aponeurosis is attached to the intersection of the rectus abdominal muscle. The action of the muscle assist the external abdominal oblique muscle (May, 1970).

2-1-4 Rectus abdominis muscle

This muscle originated from the lateral border of the sternum as far forward as the third costal cartilage. It lies side by side with its opposite muscle along the linea Alba, separated by approximately 2.5 cm. there are four or five transverse tendinous intersections crossing the muscle along its course. The muscle fiber inserted close to the Pere pubic tendon, and by lateral branches inserted into the iliopectineal eminences, with a strong attachment to the symphysis pelvis. The abdominal wall is thus strongly retracted and almost vertical at its junction with the pubis. Their action approximately similar to that of the abdominal oblique muscle, but the arching of the back is of most importance action (May, 1970).

2-1-5 Transverse abdominal muscle

It arises from the medial surfaces of the ventral ends or cartilages of the sternal ribs, meeting the costal attachment of the diaphragm, and from the transverse processes of the lumbar vertebrae by the deep layer of the lumbo-dorsal fascia. It is inserted to the linea Alba. The muscular part fibers of this muscle directed ventro-medially and are thickest near the cartilages of the rib. Caudally, it becomes very thin and fades out without reaching the pelvis. Action to retract the ribs and compress the abdominal viscera. The blood supply is from the intercostal, lumber, and musculophrenic arteries, and the nerve supply is from the lumbar and intercostal nerves (Dyce *et al*., 2009).

2-2 Hernia

2- 2-1 Definition of hernia

A hernia is defined as the protrusion of any viscus from the cavity in which it is ordinarily enclosed. As a result, a hernia cerebri is when a part of brain tissue passes through an aperture in the bony cranium. The testis may also fungate through the scrotal wall, resulting in a hernia, or fungus, testis; the lung may protrude beyond the boundaries of the thoracic cavity, resulting in a hernia of the lung; or a muscle may escape from its sheath, resulting in a hernia of muscular fibers. But the protrusion of an abdominal viscus from its position in the abdominal cavity is so decidedly more common than the extrusion of other viscera, that the term hernia,' even when employed without the qualifying adjective 'abdominal,' is generally meant to signify the protrusion of an abdominal viscus. The word 'rupture,' although no doubt used to denote protrusions through the abdominal wall, is open to the very serious objection that it implies — at any rate, in the lay mind — an altogether mistaken idea of the cause of the swelling (Verma, *et al.*,2023). The affection known as hernia generally causes considerable, and it may be, serious, inconvenience, even when it exists without complication; but if it became strangulated, a condition which may supervene at any moment, it will endanger the patient's life. The Varieties of Abdominal Hernise. In fact, no part of the parities of the abdomen can be said to be proof against a protrusion. However, some parts of the wall are much less resistant than others, and where a natural opening actually exists, the tendency to protrusion is certainly the greatest (Fossum. 2013).

An abnormal protrusion of tissue or an organ, such the bowel, through the wall of the cavity in which it normally lives is referred to as a hernia. Hernias typically affect the abdominal cavity, including the intestine, in most species, including cattle,

sheep, goats, horses, and donkeys. Most hernias are either congenital or the result of various sorts of traumas. Anatomical location, underlying etiology, and the affected organ are used to categorize hernias. Pain, discomfort, and other symptoms (Amare and Haben 2020).

2-2-2 Parts of Hernia

Hernia in general has the following parts.

1. Hernial ring: Hernial ring is a flaw in the limiting wall.

2. Hernial sac: The hernial sac is the tissue that encases the hernial contents.

3. Hernial contents: Hernial contents are any organs or tissues that have descended or shifted into an inappropriate place (Simpson, 2023).

2-2-3 Classification of hernia

Hernia classification Hernias are typically divided into several categories based on the anatomical place where they occur, including inguinal or scrotal, umbilical, diaphragmatic, perennial, pelvic, and femoral hernias. (Saiding, 2023). Hernias can also be categorized as Reducible Hernia: The hernial contents in this type can be returned manually or automatically to the abdominal cavity. Hernias that are irreducible (incarcerated) cannot have their contents reabsorbed into the abdominal cavity due to the difficulty of this kind (Thirugnanasundralingam, *et al*., 2022).

1. On the basis of anatomical site; Abdominal (umbilical and ventral) Diaphragmatic Abdominal hernia External Internal True 1.Complete sac of peritoneum surrounds the hernial content false 1.Initially do not contain a complete peritoneal sac (Bengt *et al*., 2022).

2. On basis of causative agent behind hernia Caused by trauma e.g. traumatic hernias of abdomen and incisional hernias Ventral and umbilical hernias Inguinal, scrotal and femoral hernias Perineal Inguinal (Bubonocele) Scrotal (Oscheocele) (Bengt *et al*., 2022).

3. On the basis of hernia content being Reducible or not Incarcerated and Strangulated Reducible: When the hernial contents are freely movable and can be pushed back in to the cavity. Irreducible/Incarcerated: When the hernial contents are fixed in the hernial sac due to adhesion between hernial contents and hernial sac. Strangulated: Incarceration may cause obstruction of lumen and hamper the blood supply to the herniated mass. Such type of hernia is known as Incarcerated hernia. (Bengt, *et al*., 2022).

4. On the basis of hernial Contents Intestine, liver, spleen, omentum uterus, urinary bladder, etc. (Mohsina, *et al*., 2017).

Inguinal Hernia (Bubonocele) Protrusion of abdominal contents through a defect in the inguinal ring is known as inguinal hernia.

Scrotal hernia (Oscheocele) Descendent of abdominal contents (through the defect in the vaginal ring) in to the scrotum named as scrotal hernia.

Femoral hernia protrusion of abdominal contents through the femoral canal is named as femoral hernia. Diaphragmatic hernia herniation of the abdominal viscera in to the thoracic cavity through the defect in the diaphragm is named as diaphragmatic hernia (Cokkinos, *et al*., 2011).

Hiatal hernia protrusion of abdominal contents in to the thorax through the esophageal hiatus of the diaphragm.

Perineal hernia Protrusion of abdominal and/or pelvic contents through the defect in the pelvic diaphragm (between the pelvic diaphragm and rectum).

Umbilical hernia Protrusion of the abdominal contents through the defect in the umbilicus.

Ventral hernia protrusion of the abdominal contents through the defect in the ventral abdominal wall (Fossum. 2013).

2-2-4 Diagnosis of Hernia

Different ways included in The diagnosis of hernia incloded physical examination by observation and palpation wheres clinical diagnosis represented challenging, particularly in animals who are obese, or who have scarring or adhesion on their abdominal wall Abdominal imaging may provide the first indication of the right diagnosis in these situations and confirm any suspected hernia problems(Sadan. 2019). The venteral hernia diagnosed through the identify contents of the hernia and hernia ring be clear or palpated the viscera under the skin, where the diagnosis of Irreducible hernias defaulted and needed to use the X-ray to reflect the lack of abdominal wall continuity (Muggli, *et al*., 2014).

Ultrasonography is found to have a specificity of 100% for the diagnosis of hernias, (Mohamad *et al*., 2017). Ultrasonography (US), computed tomography (CT), and traditional radiography or CT, which are cross-sectional modern imaging, helping in differentiate between different palpable abdominal wall masses and characterise hernial contents such as fatty tissue, the colon, other organs, or fluid (Lassandro *et al*., 2011).

Exploratory laparotomy also used to diagnose the defect, X-ray used to differentiate abdominal wall hernias from fibrino-cystic, abscess, and inflammatory swellings in

bovine animals (Al-Akraa, 2020). Using conventional radiographic methods, it is possible to diagnose the presence, kind, and organ involvement of hernias. Radiology, in particular, enables the diagnosis of mechanical ileus symptoms, such as the thickening of intestinal folds and the air fluid level (Francesco, *et al*., 2011). In non-emergencies, a contrast enhancement may be done using a radio opaque contrast agent (barium or water-soluble iodinated in case of obstruction or perforation) that allows gastrointestinal delineation and opacification by oral or rectal administration.

In emergency situations, a direct exam is typically performed. These techniques are useful because they allow for accurate diagnosis and can reveal any structural abnormalities, filling deficiencies, and the location and relationships of an obscured organ. Predicting future dislocation Similar to CT, US imaging identifies a mass in the abdominal wall that corresponds to the hernia sac's contents and separates it from other masses such cysts, hematomas, neoplasms, or varicoceles (Bendavid *et al*,. 2001) . In tiny midline hernias including mesenteric fat, US is especially helpful in revealing the existence of hernia symptoms. With a thorough inspection of the region and the existence of hiatal hernias, US can identify groyne hernias. The gastro-esophageal junction may also be dynamically studied. In the event of difficulties, an ultrasound may reveal the herniated organs and their effects on the peritoneal cavity, the presence or absence of color Doppler signals in the hernial contents, and whether or not the herniated organs are experiencing peristalsis. The fluid in the herniated bowel loop with thickening of the bowel wall and free fluid in the hernial sac are key indicators of imprisonment with high specificity but low sensitivity. US imaging offers an advantage over CT in the evaluation of the groyne area since it may assess the patient when they are standing and alternate between straining and relaxing(Amorosi *et al*., 2018). Because of these factors, US is extremely beneficial

for patients who have confusing or ambiguous clinical presentations. US plays a crucial role in determining the presence of complications like strangulation or incarceration because it is non-invasive, allows comparison with the asymptomatic side, and can be carried out in physiological positions with dynamic scanning. In some cases, US may also be able to detect additional pathology in the hernial sac. Limiting elements include the dependence on the operator and the rather steep learning curve. Additionally, intestinal gas hinders US performance in emergency situations, which is frequently prevalent in acute patients. A precise and comprehensive view of the abdomen is provided by CT scans, which perform better than other radiological procedures. It is possible to distinguish hernias from other abdominal masses (such as tumours, hematomas, abscesses, undescended testes, and aneurysms) and identify hernias and their contents with more accuracy using CT scans, among other benefits(Francesco, *et al*.,2011)Operator dependency and the relatively long learning curve are limiting factors. Furthermore, the presence of intestinal gas, often prominent in acute patients, limits the performance of US in emergency conditions. Among radiological techniques, CT performs better than others, providing an accurate and panoramic view of the abdomen Ultrasound (US), computed-tomography (CT) and magnetic resonance imaging (MRI) all have important roles in evaluating abdominal pathology (Caraiani.*et al*., 2020). Advantages of CT include more accurate identification of hernias and their contents and differentiation of hernias from other abdominal masses (hematomas, abscesses, tumors, aneurysms and undescended testes) (Francesco, *et al*., 2011). Additionally, multi-detector row CT may aid in identifying subtle symptoms of complications within the hernia sac, such as intestinal obstruction, strangling, incarceration, and traumatic wall hernia because to its better anatomic detail. CT is helpful for assessing post-operative patients, particularly those with enlarged lumps or flamboyant scars. Position, The shape and content of abdominal wall hernias are all better understood

in obese patients when using CT The primary investigation of abdominal herniations in tradtional radiography, US, and CT examinations are the subject of many work. (Aguirre *et al*., 2004).

Umbilical hernias must be differentiated from other affection and lesions as umbilical mass (Coste, *et al*., 2023).

The diagnostic strategy for hernias should very rarely involve diagnostic laparoscopy because it is an invasive procedure. However, when imaging is inconclusive or cannot be used to evaluate for an occult hernia be acquired. Diagnostic laparoscopy makes things easier Identification of intra-abdominal hernias and other pathology (Campanelli, 2022).

2-2-5 Herniorraphy and Hernioplasty

2-2-5-1 Principles of treatment of hernia

1. Reposition of hernial contents in to their normal anatomical position.

2. Closure of the hernial ring either by applying sutures or by mesh (in large hernias).

3. Closure of skin and subcutaneous tissues (Fossum. 2015).

2-3 The mesh

2-3-1 Surgical meshes history

Since 1891, surgical meshes have been used to repair hernias, but post-surgery problems like infection, fibrosis, adhesions, mesh rejection, and hernia recurrence have led to research on various materials, production technologies, and surgical procedures. Surface modification approaches and nanofiber-based systems are being

investigated for material strength and biocompatibility. Theodor Billroth proposed a prosthetic material for hernia repair in 1890, but multifilament suture material was ineffective in various surgical operations (Billroth, 1924; LeBlanc, and Booth, 1993; Greenberg and Clark 2009; Chowbey, 2012; Baylón, *et al*., 2017). Dr. Francis Usher researched materials to ease hernia repair problems, but Nylon, Orlon, Dacron, and Teflon were rejected due to issues like foreign body reaction, sepsis, stiffness, fragmentation, and loss of tensile strength. In 1955, he discovered Marlex, a highly effective polyolefin material, which allowed for tissue integration and increased collagen production. In 1958, he published his polypropylene mesh surgical approach, which later became popularized as the Lichtenstein repair or tension-free mesh technique. (Usher b *et al*., 1959)

The European Union Hernia Trialists Collaboration conducted 58 randomized controlled trials in 2002, showing that surgical meshes were superior to other methods in reducing recurrences and postoperative discomfort. Mesh mending decreased the incidence of hernia recurrence in cases of ventral hernia repair and inguinal repair using surgical mesh. (Klinge, *et al*., 2002).

Currently, most surgeons agree that the best method for treating hernias is using prosthetic mesh. However, the biocompatibility of the material plays a significant role in the effectiveness of repair. Mesh implantation can lead to a stiff scar and poor tissue incorporation, leading to hernia recurrence or mesh infection. Surgery remains the only available treatment, but improved surgical techniques like laparoscopic surgery can reduce postoperative side effects. (Carbajo et al., 1999).

(EU Hernia Trialists 2002). They specifically saw fewer recurrences and decreased postoperative discomfort with mesh mending other trials that validated these outcomes showed that hernia repair utilizing Compared to hernia reconstruction,

surgical meshes decreased the incidence of hernia recurrence through in cases of ventral hernia repair, 2.7% vs. 8.2%, and by 50-75% of improvement through Inguinal repair using surgical mesh Today, the majority of surgeons concur that the best method for treating hernias is to utilize a prosthetic mesh. It should be noted that in the past, the strength and permanence of the mesh itself were used to determine the effectiveness of repair rather than the amount of scar tissue or other factors that later appear in and around the mesh (Gilmore, 2015). The prosthesis was rejected because of the formation of scar tissue by the immune system, and the biocompatibility of the material has been shown to have a significant role in this. When a surgical mesh is implanted and is not properly biocompatible (either due to the material it is made of or its structural design), the body reacts by encasing the foreign system, which results in the formation of a stiff scar and poor tissue incorporation, which can lead to hernia recurrence or mesh infection. The need to remove a lot of meshes arises from the fact that 69% of explanted meshes are a result of prosthesis infection (Hawn *et al*., 2011).

2-3-2 Types of meshes

Recently, for reconstruction the abdominal wall defect many researchers suggested many types of prosthetic materials. The various types of meshes are all intended to accelerate the healing process during achieve a free- tension closure by use to reduce the frequency of recurrences and complication rates (Rathore *et al*., 2018). Polyethylene mesh is the first mesh used in reconstruction of ventral in 1958 as a synthetic polymeric non-restorable (Miserez *et al*., 2019).

2-3-3 Polypropylene mesh (PP)

In hernia surgery, mesh has proven to be a better choice than sutures for strengthening the fragile abdominal wall. As a result, numerous attempts have been made to improve the host body compatibility of this fiber-based mesh. Researchers have investigated various materials, designs, and manufacturing methods to enhance the surgical meshes on the market now. In additiony various biomechanical systems have been modified and developed through surface modification implant mesh characteristics (Saha *et al*., 2022). Since 1891, surgical meshes, particularly those used to repair hernias, have been in use. Given the numerous post-operative complications, including infection, fibrosis, adhesions, mesh rejection, and hernia recurrence, study in the field has since grown. Scientists have centered on the implementation and analysis of a variety of materials: combines with various different manufacturing processes, a range of surgical and medical applications, as well as fiber size and porosity methods for implantation currently, surface modification techniques and nanofiber development based systems are being extensively investigated as potential areas to maintain material strength and boost the mpatibility of the meshes currently in use (Baylon, *et al*., 2017).

2-3-3-1 Tensile strength

A hernia mesh must have strength as its primary requirement. To add the necessary reinforcement, the mesh is implanted into the weak abdominal wall. As a result, the mesh needs to be strong enough to provide the necessary strength. The recommended maximum loads for the abdominal wall after hernia repairs are 22 N/cm and 32 N/cm in the lineal and lateral orientations, respectively (Pott *et al*., 2012). The maximal load felt in the groin is 16 N/cm, which is significantly less due to its anatomy (Zhu, *et al*., 2015). Regardless of their weight or structural makeup,

most synthetic meshes exhibit a tensile strength of at least 32 N/cm, which qualifies them to strengthen hernia defects. Implanted mesh, however, may potentially demonstrate diverse reinforcing abilities in vivo contexts (Cobb1, *et al*., 2006).

2-3-3-2 Explosive power

In order to expand the mesh to the point of rupture under accepted testing conditions, the mesh must be subjected to a maximum uniform pressure at a right angle to its plane (Deeken and Lake 2017). An essential mechanical characteristic is burst strength. Specifically for knitted mesh, since knitted mesh has a flexible composition and can extend in multiple directions. The mesh that was inserted could depending on their actions, such as walking, coughing, or sitting, patients are put under various stress conditions in the belly. Standing during mating mesh implants will perform poorly and have a higher risk of hernias if their burst strength qualities are lost reappearance as a result, care is given to the mesh's flexibility and bursting strength. Most synthetic materials knitted meshes showed higher burst strength than the average burst strength of abdominal wall fascia, (Cobb2. *et al*., 2005: Sanbhal *et al*., 2018).

2-3-3-3 Size and density of pores

In a mesh fabric, porosity is defined as the ratio of the mesh voids to the mesh voids' combined volume (Saha, *et al*,. 2022) When integrating the mesh into the body properly following hernia surgery, porosity, pore size, and pore shape all play crucial roles (Lake, *et al*., 2015). Usually, when a mesh is inserted into a body, the inflammatory reactions begin to develop granulomas, usually around individual mesh fibers. Later, the separate granulomas combine to wall the implant by covering the pores and forming a protective layer. Bridging refers to this technique, which impedes tissue ingrowth and stiffens the scar plate, which decreases flexibility

(Casey, 2015). Meshes with Pores larger than 2 mm are connected in a loose network. Unlike the tiny hole, however Large pore size (>2mm) meshes are connected in a loose network. Contrarily, meshes' modest pore sizes promoted the growth of bridges (Jerabek, *et al*., 2014). Orenstein, *et al*., (2012) found that meshes with big pores had reduced fibrosis. Large-pored mesh improves fluid transmission, mechanism that speeds up healing through the pores and reduces postoperative seroma (Orenstein *et al*., 2012). Furthermore, bacterial growth and cell proliferation are influenced by the porosity of the material and the size of the pores. Meshes with large pores allow macrophages, fibroblasts, collagen fibers, and other immunocompetent cells to easily invade. The infiltration of fibroblasts and collagen fibers stimulates the creation of connective tissue, which leads to correct integration into the bodily system. The other hand, Infiltration of macrophages and other immunocompetent cells reduces the risk of infection by preventing bacterial colonization (Vindal, *et al*., 2022) at the implant site biocompatibility is proportional to mesh pore size, meshes with a tiny pore size (10 m), there is a risk of inflammatory reaction, inadequate cellular activity, and infection, which leads to rejection of the mesh inserted (Sanbhal, *et al*., 2018).

2-3-3-4 Weight (Density)

The weight of an implant is an important factor to consider since it promotes proper integration into the body with minimal inflammatory responses. It has been found that a low inflammatory response is critical for improved tissue integration and wound healing (Zhu, *et al*., 2015). If the mesh weight is heavy, may predisposed of greater inflammatory reactions than the lightweight implant. As a result, lightweight meshes with lower materials provide a limited inflammatory response, resulting in better tissue integration and enhanced prosthesis compliance. Furthermore, lightweight meshes with larger pores are usually more elastic, resulting

in reduced pain and discomfort after implantation (Sanbhal, *et al*., 2018). There is no evidence to support a connection between receiving a PP mesh implant and developing autoimmune diseases (Kowalik, *et al*., 2022).

2-3-4 Future plans

Hernia repair mostly relies on the use of surgical mesh for therapy, which, is not ideal, for any time and has a lower recurrence rate. As a result, many study is being conducted to develop the next generation of surgical mesh, with an emphasis on addressing some mesh application concerns, focusing on biocompatibility, adhesion, and infection control. Nano fibrous barrier, hydrogel in the biological field, mats and surface coating with appropriate polymers and nanoparticles have shown very encouraging results. Mesh performance despite extensive research in this field and advances at lowering the recurrence rate, current meshes continue to be problematic. Suffer from post-infection, intestinal blockage, and organ adhesion treatment the most sought-after topic in hernia mesh research is still the development of an optimum hernia mesh (Saha.*et al*., 2022).

2-3-5 Mesh locations:

There are several location of surgical mesh to be implant;

(A) **Onlay;** When the mesh is positioned between the subcutaneous tissue and the anterior rectus sheath, it is said to be implanted on-lay (Hiekkaranta *et al*, .2023).

(B) **Inlay;** Implanting an inlay is when the mesh is positioned between the abdominal layer's borders tissue where the defect is. The mesh is fastened to the edge of the defect, creating a bridge to close the hole (Hiekkaranta *et al*., 2023).

(C) **Sublay;** The mesh is implanted below the repaired muscle, which is known as sub-lay implantation. This could be between the back between the peritoneum and

the rectus muscle or between the rectus sheath and the muscle Sheath/muscle of the posteriorrectus (preperitoneal). (Messer, and Rosen, 2023).

(D) **Under-lay**; Mesh is inserted into the abdominal compartment and laid on the anterior abdominal wall deep to the peritoneum. Often bridging especially in laparoscopic surgery (Parker, *et al*., 2017) (fig. 2-1).

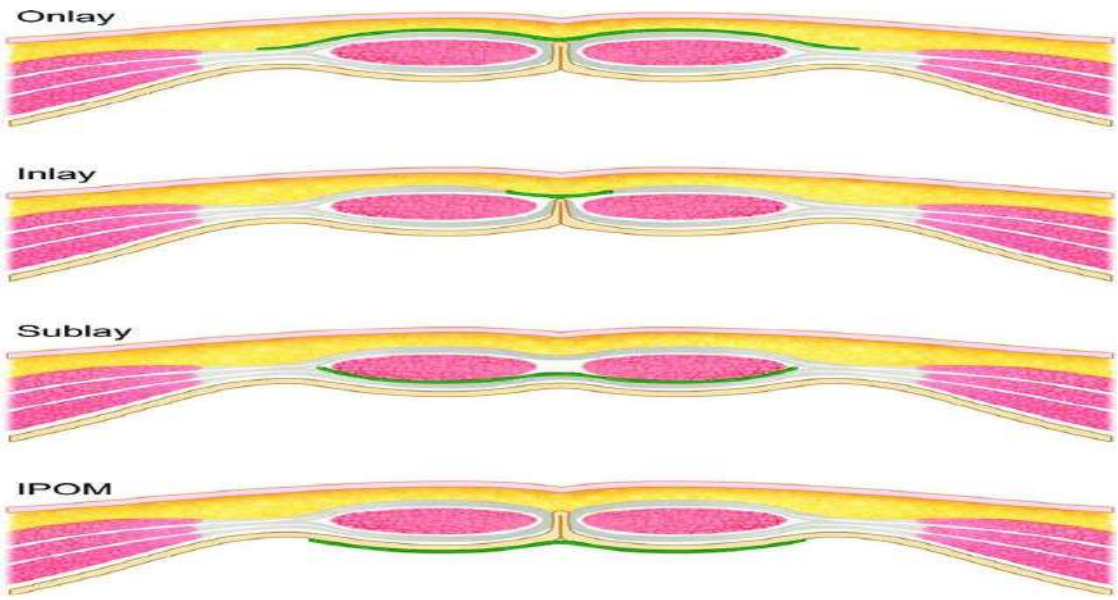

Figure 2-1: illustration shows different techniques of mesh repair for incisional or ventral hernia according to the location of mesh placement. Available via license: CC BY-NC 4.0 Content may be subject to copyright (Choi, and Lee, 2018).

In hernia surgery, mesh has proven to be a better choice than sutures for strengthening the fragile abdominal wall. As a result, numerous attempts have been made to improve the host body compatibility of this fiber-based mesh. Researchers have investigated various materials, designs, and manufacturing methods to enhance the surgical meshes on the market now, in addition Various biomechanical systems

have been modified and developed through surface modification mesh implants' characteristics (Saha *et al*., 2022)

Modern repair of IH (diameter > 1 cm) involves reinforcement with a prosthetic mesh. This has reduced the number of recurrences seen when performing suture repair (Köckerling *et al*., 2021).

2-4 Laparoscopic hernioplasty

Laparoscopic ventral hernia repair is performed less frequently than open repair because some ventral hernias are unsuitable for laparoscopic repair and the complications are more severe than those of open repair. The technique for laparoscopic ventral hernia repair depends on the shape, size, location, number, recurrence, and symptoms of the hernia. Complications of laparoscopic ventral hernia repair include seroma, hemorrhage, intestinal injury, mesh infection, and recurrence (Park and Chung 2017).

In laparoscopic abdominal hernia repair, mesh placement methods are generally classified into intraperitoneal onlay mesh (IPOM), transabdominal preperitoneal (TAPP), and totally extraperitoneal (TEP). IPOM is the most frequent technique used for laparoscopic ventral hernia repair, and the mesh is located just under the peritoneum. Therefore, mesh and organs may contact directly leading to a high rate of adhesions and other surgical complications. The TEP and TAPP procedures are the same as the procedure used for inguinal hernia repair. The mesh is located between the abdominal wall muscle and the peritoneum, without direct contact between the mesh and intraabdominal organs. However, as the operative space is narrow and restricted, there is a high possibility that endoscopic instruments will collide with each other during the operation, thereby increasing the effort and

time required to accurately deploy the mesh in the narrow surgical field (Mitura *et al*,. 2017).

First described by LeBlanc and Booth (LeBlanc and Booth 1993), laparoscopic intraperitoneal onlay mesh (IPOM) repair is currently regarded as a standard surgical treatment for ventral hernias (VH). IPOM has a number of evident benefits over the open method, including a low rate of wound complications and a quick recovery. It has some restrictions, though. According to (Bittner *et al*., 2019), it is connected to uncommon but severe complications that may occur after intraperitoneal mesh placement, such as visceral damage, ileus, mesh migration or mesh erosion, and enter cutaneous fistula brought on by direct contact between the mesh and intraperitoneal viscera (Yang 2017)

Incisional hernia repair using the on-lay and sub-lay mesh techniques had acceptable complication rates and did not significantly differ in terms of post-operative complications (Magis *et al*., 2021).

When treating paraumbilical hernias, the on-lay mesh repair approach is superior to the sublay mesh repair technique in terms of effectiveness, speed, and safety (Prakash *et al*., 2022).

2-5 Mesh Fixation

Mesh fixation in hernia surgery is controversial, with most commonly using sutures, cyanoacrylate glues, and fibrin. Non-fixation methods are favored, and Lichtenstein approach is popular. (Lichtenstein *et al*., 1989). The Lichtenstein procedure uses a Prolene overrunning suture to secure mesh to muscles, with absorbable stitch materials like Vicryl to reduce nerve entrapment risk. It has positive literature results. (Zhang *et al*., 2021). However, a number of recent studies

revealed a high prevalence of chronic pain, with an average incidence of 12% and occasionally as high as 53% (Bay-Nielsen *et al*., 2001; Bay-Nielsen *et al*., 2004).

Only a few research examined the social consequences of chronic pain following hernia repair, despite the fact that many considered chronic postoperative pain to be a surgical primary outcome. Up to 6% of patients with this persistent groin pain have indicated that it has an impact on their social and professional lives (Poobalan *et al*., 2001; Bay-Nielsen, *et al*., 2001; Kehlet and Wilmore 2008 and Ruiz-Jasbon *et al*., 2020). Chronic groin pain can result from persistent inflammation in the Lichtenstein operation, including foreign body over-reaction, pubic tubercle periosteum inflammation, and nerve entrapment in the suture. (Helbling and Schlumpf 2003). The Lichtenstein method is a tension-free technique, but stitches can cause strain and stiffness in the inguinal region, leading to postoperative pain and slower recovery. To prevent these issues, tissue-compatible glues have been used, which are biocompatible, affordable, and convenient to store and use. They reduce postoperative pain, increase hemostasis, and speed up the procedure. Fibrin glues mimic the coagulation cascade. (Narayanaswamy *et al*., 2023). Fibrin glues are utilized in a range of surgical procedures as a tissue adhesive. Fibrin glues' key benefits are tissue compatibility, biodegradability, and effectiveness when used on wet surfaces. Some publications have criticized the possibility of contamination by transmissible blood-borne pathogens (De Hingh *et al*., 2009). Both open and laparoscopic techniques to fibrin glue have produced excellent outcomes in the fixing of tension-free mesh (Schwab *et al*., 2006; Ortillés *et al*., 2017). Long-lateral-chain cyanoacrylates (CAs) are preferred by surgeons for open mesh repair for hernias due to their affordability, ease of storage, and ease of use. (Tebala 2015). Experimental models show increased inflammatory response from CAs doesn't significantly alter collagen maturation or delay mesh integration. No studies

distinguish M1 and M2 macrophages, suggesting some cells may be reparative, unlike M1 causes inflammation. (Pascual *et al*., 2018).

2-6 Complications of mesh hernioplasty

2-6-1 Adhesion

The postoperative adhesions is the most prevalent problem occur after repairing hernia There are abnormal fibrous connections in non-anatomic parts within animals body. Many causes of postsurgical adhesion including thermal damage, trauma, infection, ischemia, and implant foreign materials like mesh and suture materials (Klinge *et al*., 1999; Liakakos *et al*., 2001).Postoperative adhesions are associated with foreign materials and elements between the site of operation and viscera inside the body in about 61% and 69% rate of cases (Bouliaris 2019; Liao and Fan 2023).

The implanted mesh something improperly adherent to the adjacent tissue or viscera in about 80% of all repaired cases (Yeo and Kohane 2008). As a part of the normal healing process immediately post-surgery, the trauma occurs which directly followed by formation exudates rich in fibrin and this is the major reason of transient adhesions. It’s eliminated by the fibrinolytic system. However, inflammation, ischemia, or the presence of foreign materials impedes the absorption of fibrin (meshes). As a result, even years after the surgery, the temporary adhesions develop into heavy tissue adhesions and cause many problems and difficulties. The adhesion can result in excruciating pain, restlessness, discomfort, a need for further surgical interventions, significant treatment, additional costs, at its worst, intestinal obstruction internal disturbance which could be deadly (Yeo and Kohane 2008;Brown and Finch 2010;Bouliaris *et al.*, 2019).

The effectiveness of various surgical correction procedures, such as inlay versus onlay, has not been proven beyond a reasonable doubt adhesion development (Dreger *et al.*, 2019). Additionally, laparoscopic surgery has increased the worry about mesh adhesion issues (Brown and Finch 2010).

2-6-2 Fistula

One of the most causes of enterocutaneous fistula is placement of mesh during hernioplasty close proximity to bowel components such the intestine or stomach (Sistla *et al.*, 2008). So, the stomach and intestines are more likely to pass out. It poses a danger and a bad warning to the animal. There is a ratio with a 10% mortality rate, mesh-related fistulation that develops after the hernia mesh may be mortal (Eriksen *et al*., 2007). There have been many reports of fistula formation following intraperitoneal placement of PP mesh via open ventral hernia repairing (Eriksen *et al*., 2007; Najm *et al*., 2023).

2-6-3 Infection

These included symptoms of swelling, redness, pain which are consider as the characteristic feature of inflammatory reaction. Fever, scorching discomfort, and soreness one of the worst issues that may develop right away following surgical repairing of hernia (Pande and Naidu 2020). There are necessitates of surgical removing the diseased mesh, when mesh infection is suspected. Infection is the reason for around 69% of mesh explant instances (Hawn *et al*., 2011). The infections my not impotent when it is superficial. And my treated with antimicrobial agent and subsided during few days post treatment. Occasionally outcome in formation of deep abscess and deal with it as emergency case. Which need a second operation (Köckerling 2019).

Many factors contributed in developing mesh infection as type of operation, time consuming as well as structure mesh's (Christou *et al.,* 2020). More surface is provided by multifilament and porous mesh may contribute in bacterial adherence and micropore-containing structures (10 m), inhibits the action of immune cells and making it difficult for these cells to remove bacterial (Eriksen *et al.,* 2007;Brown and. Finch 2010). Some mesh materials are somewhat prevent spreading bacterial infection since they don't attract bacteria. The surgical procedure also plays a significant role in the situation of the formation of infection. The workers records about 6-9% of infection incidences following open ventral hernia repair (Eriksen *et al*., 2007). Laparoscopy now is the slandered devise for examination and treatment method which permits visualization, and reduce risk of bleeding less time consuming and prevent infection and adhesions (Awaiz *et al*., 2015). It contributed positively in reducing the risk of infection as a compare to open ventral hernia repair according to (Kirshtein *et al.,* 2002; Kua *et al*., 2002; Lomanto *et al*., 2006).The using hand -assisted laparoscopy used now as alternative method for repairing hernia and contributed in sealing incision this played a role in preventing leakage and serious contamination (Wolak *et al.,* 2021).

2-6-4 post-operative pain

There are several reasons that lead to pain afterward surgery as foreign materials reaction, immune rejection, nerve injury, bacterial contamination and subsequence Infection and shrinking, (Brown and Finch 2010; Eriksen *et al.*, 2007). Nerve trauma and damage may cause pain immediately afterward surgery. Chronic pain subjected by a reaction to a foreign materials. Meshes typically guarantee a repair without tension, which causes less discomfort than suture repair (Brown and Finch 2010). Also, chronic discomfort is outcome of using meshes and it’s very concerning to the structure and material qualities which play a vital role in foreign

body reactions. And the incidence is approximately 30% of patients experience chronic pain (Kumar *et al.*,2002).As example of chronic pain, the pain occurs following inguinal hernia the symptoms after surgical correction included Sharp or radiating (spreading) pain, a burning sensation in the area of the surgery, Foreign materials sensation pain in the testicles (Bande *et al.*, 2020).

2-6-5 Recurrence

It mean recurring hernias at the same site or neighboring site just close to the site of operation after reconstituting hernia the recurrence concern at this situation. In case of laparoscopic ventral hernia repair (LVHR) the rate of recurrence might be reach to 1 and 17% (Eriksen *et al*., 2007).Recurrence can also occur as a result of a variety of factors, such as the structural and mechanical integrity of the prosthesis that was used size of the hernia, an inexperienced surgeon especially during hernioplasty, small size of incision, mesh overlap, A history of post-operative infection, seroma, and last meal of medication (Awad *et al*., 2005;Eriksen *et al*., 2007).In case of mesh's strong reinforcement capacity, the recurrence rate has significantly decreased. A report claims that the occurrence from 17 to 67% to 1-32% (Brown and Finch 2010). The rate for incisional hernia has decreased. Re-herniation is typically visible along the borders of the implanted mesh as a result of inadequate fixing or severe mesh shrinking. (Awad *et al.*, 2005).

The faulty in collagen production is a significant reasons involved in the recurrence of hernia (Brown and Finch 2010). The ratio of Type I to Type III collagen synthesis is affected by the foreign body reaction, which alters the surgical site's tensile strength and mechanical stability. Additionally, there are relationship between recurrence and collagenous tissue production which have been recorded many literature (Eriksen *et al.*, 2007; Totten *et al.*, 2019). Recurrence is related to

multifactor, making it difficult to connect recurrence to mesh material. In recent study done in rat model, the recurrence rate for PP mesh was found to be considerably lower than ePTFE mesh after 8 weeks in a hernia repair (open surgery) (Kingsnorth 2009).Whereas another worker observed that during two years of implantation in human subjects (n=265), PP mesh exhibits a considerably lower recurrence rate of 4.05% (6 instances) than pollster (PE) mesh (Socea *et al*., 2018).

2-6-6 Seroma

A seroma is a swelling area of an organ brought on by the accumulation of clear fluid. As a result of inflammatory reactions and hemorrhages seroma may develop following a hernia. The incidence of seroma generation after laparoscopic ventral hernia repair (LVHR) surgery has been found to different percentage (0.7–93%) (Eriksen *et al*., 2007).The seroma vary according different factors according to its definition, approaches, and timing of seroma which determine measurement of seroma after the surgery. In one of the studies one week post-surgery, seroma occurred in all patients who underwent LVHR with ePTFE mesh. Of these, 35% experienced aches and pains, and 20% had chronic seroma for as long as three months (Susmallian *et al*., 2001).

2-6-7 Shrinkage

Shrinkage after implantation or an adjustment in the mesh's dimension—considered as problematic in case of hernia. From a material standpoint, the mesh may experience some slight shrinkage in bodily fluids. Weight, pore size, and mesh type may all affect how much the material shrinks (Eriksen *et al.,* 2007; Silvestre *et al*., 2011). Small-pored heavyweight mesh revealed larger scar plate and more shrinkage (Brown and Finch 2010). When compared to other options, such as PE and PTFE, (Judge *et al.,* 2007; Novitsky *et al*., 2007) reported that PP mesh performs

better in terms of lower shrinkage. According to the previous studies, light PP mesh with a large pore size experiences the least amount of shrinkage after implantation. The mesh is not contracted as itself, However, It happens once the scar tissue contracts (Zogbi *et al.,* 2013). In other words, the tightening of scar tissue, the scar plate, an infiltrating pile layer made up of macromolecules and cells, leads the neighboring mesh to contract.

For the abdominal wall to move normally the in vivo environment, the mesh's dimensional stability is most crucially, for effective tissue integration, this occur due to failure of the mesh, which is the worst outcome of mesh shrinking (Sanbhal *et al.,* 2018).

The granulomatous layer develops this due to significant inflammatory response in the body which caused by the implanted mesh and the fibers bonds them together to create a scar plate. The scar plate causes a firmer stomach wall that interference with digestion (Cobb *et al.,* 2005; Sanbhal *et al.,* 2018). Other issues such as recurrence of post-operative pain that could result from shrinkage after implantation (Zinther *et al*., 2010; Nohuz *et al.*, 2014). Pointed on the effects of laparoscopic approaches placement of various meshes relating to shrinking during prolonged implantation in a ruminants (sheep). In the study using coated polyester and covered polypropylene meshed with anti-adhesive material three months after implantation, the Results exhibited low degree of shrank in about 20% and 41%, respectively, Regarding shrinkage with significant appearance after few hours and different appearance in 18 months later (Zinther *et al*., 2010). Another workers pointed that the open hernioplasty with of polypropylene mesh shrank less than polyester mesh (Socea *et al.,* 2018). In a human experiment, Silvestre et al. found that after 90 days of implantation, heavyweight PP mesh shrank more than lightweight PP mesh (Silvestre *et al*., 2011). In an effort to determine the relationship between adhesion

and contraction, (Hu *et al.,* 2018) founded that the effectiveness of two anti-adhesives to stop PP mesh shrinkage: Seprafilm®, a bioresorbable membrane based on hyaluronate carboxymethyl cellulose, and Hyalobarrier® gel, an autocross-linked polysaccharide hyaluronan solution. With a barrier in place instead of PP alone, the results revealed a significantly lower mesh shrinkage and adhesion score. Therefore, it is clear that mesh shrinkage and anti-adhesive property are connected.

2-7 Aloe Vera

Aloe Vera is a plant that categorized to family, called Liliaceae that life in dry and hot areas. Its grow in abundance in African, Asia, Europe and America regions (Bhuvana *et al*., 2014). Aloe Vera is utilized for numerous therapeutic applications. It naturally contains a variety of valuable chemicals with the potential to be used in the treatment of numerous ailments. Sugar, enzymes, saponins, vitamins, aloeemodin, aloesin, aloin, acemannan, aloeride, aloemannan, flavonoids, methylchromones sterols, naftoquinones, minerals, amino acids, anthraquinones, salicylic acid, lignin, and other various compounds, including fat-soluble and water-soluble vitamins, enzymes, minerals. Aloe Vera is used as antifungal and antibacterial bioactive materials against different pathogenic fungal and bacteria strains (Danish *et al.*, 2020).

Aloe Vera's such as Aloe arborescens, Aloe ferox, Aloe barbadensis and Aloe Vera are a few of the Aloe species that have been studied. Aloe Vera, a permanent green herb of the Liliaceae family, it is the vary in most effectiveness on healing wounds process. At the top of the stem, in clusters, are the large, juicy leaves. The lanceolate leaves have tiny spiky teeth along the edges of leave. The flowers of this plant are red, yellow, or red-spotted. It is now a widely-cultivated multipurpose crop that is planted all over the world. It has a free range of beneficial values,

including those as oxidative agent against cancer, lipid-lowering, hypertension, bacteria, and diabetes, inflammation, immunological control, liver protection, viruses, ulcers.(Ogidi and Enenebeaku 2023).

Different studies have exhibited that the pharmacological effects of more than 200 biologically active chemicals, including anthraquinones, anthrones, carbohydrates, flavones, chromones, amino acids, alkaloids, vitamins, lipids, as well as minerals, are due to the interactions of these chemicals agent. The leaf of Aloe Vera is commonly used in medical applications. Three components comprise an Aloe leaf. Green leaf epidermis makes up the top layer. In the layer, there is phloem and xylem. In contrast to the phloem, which is engaged in the transportation of tiny organic matter and carbohydrates, the xylem is in charge of moving water. The reddish-yellow latex, which is produced by pericyclic cells under the cuticle of the leaf epidermis, makes up the middle portion. Anthraquinone, which is its primary active component and comprises which includes chrysophanol, aloin, emodin. Antioxidant properties of the extract of Aloe Vera leaves when injected intra paretonil (Matti *et al*., 2010).

2-8 Platelet Rich Fibrin (PRF)

(PRF) has been referred to as a second-generation autologous platelet concentrate. PRF biological characteristics, on the other hand, differ significantly from those of PRP and cannot be regarded as a PRP development but rather as a new bio stimulator. The patient's venous blood is taken in regular glass tubes, and the manufacture of PRF starts with an instantaneous centrifugation of that blood. The procedure was initially explained by (Choukroun et al., 2006; Mehta *et al*., 2018). PRF (Marx *et al*., 1998) introduced platelet-rich plasma, the first platelet concentrate, in 1998. PRP has been utilized in conjunction with bone grafts in

dentistry, surgery, and for cosmetic and orthopedic purposes to try and repair osseous defects (Kobayashi *et al*., 2017; Kardos *et al*., 2018). PRP has also been utilized to facilitate gingival, cutaneous, and skin wound healing as well as to speed up soft tissue regeneration. Osteoarthritis treatment using PRP injections is also available (Fujioka-Kobayashi *et al*., 2017; Bahadoram *et al*., 2023). Its downsides include the inconsistent methods used to prepare PRP, the use of bovine thrombin in the activation step, and—most significantly—the brief period of target tissue stimulation. An autologous biomaterial called PRF is constructed of a robust fibrin matrix with varying amounts of High levels of platelets, leucocytes, and circulating MSCs—both vital and non-vital—are present. A higher level of long-releasing growth factors (GFs). These include connective tissue growth factor (CTGF), bone morphogenetic protein 2 (BMP-2), transforming growth factor (TGF -1, 2), insulin-like growth factor (IGF-I), and platelet-derived growth factor (PDGF A-B) (Dohan Ehrenfest *et al*., 2012; Dhurat and Sukesh 2014). Elevated levels of fibrin, fibronectin, vitronectin, and thrombospondin; fluctuating heat shock protein HSP concentrations (not well studied yet) the complex process of tissue regeneration is mediated by a wide range of biochemical and immunological events, which are controlled by different cytokines, tissue mediators, and growth factors (GFs). Although it is recognized that cells of different lineages generate these molecules, the details are not well known. Platelets play a key role as an autologous source of growth factors (Saluja *et al*., 2011). Since their activation, platelets secrete multiple GFs including PDGF, TGF β-1, 2, and IGF-I (Naik *et al*., 2013). To reduce inflammation and hasten the healing process, autologous platelet concentrates are frequently employed as a bioactive surgical component. Platelet concentrates can now be made from blood using a variety of methods that have been developed in recent years (Kardos *et al*., 2018). PRF creation: Both the price and the procedure are reasonable. In sterile, plastic-coated tubes (8–10 ml in size), blood samples are

drawn from the patient and promptly spun in a centrifuge. Various centrifugation techniques are described in the literature in order to produce diverse types of PRF with various characteristics. A-PRF (Advanced Platelet Rich Fibrin) and L-PRF are two well-researched PRF products (Leucocytes Platelet Rich Fibrin). By modifying the features and processes of centrifugation, certain PRF biological qualities can be produced. The final PRF's characteristics and quality are determined by the centrifuge's stability, vibration, and the temperature that develops in the tubes. Particularly, L-PRF clotting and membrane formation are influenced by centrifuge parameters, which in turn affect cell survival, fibrin architecture, and the presence of GFs (Dohan Ehrenfest *et al*., 2012). The A-PRF clots and membranes seem considerably smaller, more brittle, and less separated from the red blood cell layer than the L-PRF membrane. The original L-PRF exhibits a heavily polymerized thick fibrin matrix and numerous cells, including activated lymphocytes, appear to be alive and normal in shape (Madurantakam *et al*., 2015). The majority of the visible cell bodies appear damaged or destroyed, and the A-PRF displays a thin, lightly polymerized fibrin gel. A-PRF membranes dissolve in vitro in less than 3 days, and their GFs rapidly dissipate or drop (Naik *et al*., 2013;Dohan Ehrenfest *et al*., 2012). In addition, L-PRF membranes in vitro maintain good health for 7 days and release their growth factors gradually for at least 7 days. After centrifugation, through the activation of autologous thrombin, a fibrin clot is created. Three distinct layers can be seen in the tube red blood corpuscles RBCs at the bottom of the tube, platelet-poor plasma PPP on the top of the tube, and the PRF clot in the middle of the tube. Surgical tweezers can be used to remove the PRF clot from the tube. By gently compressing the clot, it is possible to push out the exudate, which is abundant in growth factors and found in large quantities in the clot itself, to produce PRF membranes. Hyper-acute serum, which is squeezed out of the PRF clot, has a higher proliferative effect on many connective cell lineages, including bone marrow

mesenchymal stem cells (MSCs), osteoblasts, and chondroblasts cells (Cortellini *et al*., 2018). The remaining PRF membrane is a three-dimensional, sticky, biocompatible, and biodegradable scaffold once the hyper-acute serum portion has been removed. Contact and cell interactions are facilitated by the membrane surface and ECM structure. Additionally, PRF membranes have the capacity to gradually release bioactive compounds that promote the migration, adhesion, and proliferation of nearby MSCs (Boora *et al*., 2015; Kardos *et al*., 2018; Di Liddo *et al*., 2018). Three distinct layers can be seen, with red blood cells (RBCs) at the bottom, platelet-poor plasma (PPP) at the top, and a PRF clot in the center. The PRF clot can be taken out of the tube using surgical tweezers. Centrifugation transforms the plasma's soluble fibrinogen into fibrin, which polymerizes into a three-dimensional structure. The fibrin net traps the activated platelets and some leukocytes. As a result, upon activation, platelets and leukocytes create a storage pool of growth factors (Varela et al., 2019). On the outside and interior of the PRF membranes, platelets can be seen. One of the more well-known GFs produced by platelets, PDGF, promotes MSC adherence and proliferation in soft and bone tissue regeneration (Kardos *et al*., 2018). MSCs seeded onto PRF membranes quickly proliferated on the surface of fresh membranes, but even better on freeze/thawed or freeze-dried membranes. The structure of fibrinogen, the stability of membrane bio factors, or the clinical usefulness of the PRF appear unaffected by freeze-drying (Miron *et al*., 2017). As a result of their tensile strength, which can hold a suture, and potential suitability for various surgical procedures, freeze/thawed or freeze/dried membranes are advantageous for wound closure. In addition, freezing the membranes at −20°C and thawing at +4°C may help to slow down the process of membrane degradation. Therefore, some Authors observed that exposing injured tissue to prolonged membrane stimulation enhances the effectiveness of tissue regeneration (Kardos *et al*., 2018). However, it is intriguing to note that only fresh membranes have living

cells, whereas frozen and freeze-dried membranes have only dead cells (Li Q *et al*., 2014). The HSPs concentration created during the freezing process may contribute to the tissue regeneration of freeze-dried membranes (Di Nicola 2020). Clinical applications of PRF include the treatment of non-responding skin ulcers such as venous leg ulcers (VLUs), pressure ulcers (PUs) and diabetic foot ulcers (DFUs) (Pinto *et al*., 2018). The high concentration of platelets and leucocytes, along with the prolonged release of growth factors, can be used to explain why L-PRF membranes have an advantageous influence on the healing of chronic leg ulcers. To speed up the healing process, it appears to be essential for growth factors (such as TGFß-1, TGFß-2, PDGF-AB, VEGF, EGF, and CTGF), matrix glycoproteins (such as thrombospondin-1, fibronectine, and vitronectine), inflammatory regulators like cytokines, and various HSPs to release gradually over a number of days (Dohan Ehrenfest *et al*., 2009; Dohan, Ehrenfest *et al*., 2012). The use of PRF membrane in dentistry and maxillofacial surgery is common. The treatment of periodontal bonydefects and regeneration, ridge preservation, sinus-floor elevation, implant surgery, and the construction of the PRF bone block are just a few of the documented treatments (Bakhtia *et al*., 2017). In an effort to speed up meniscal repair, Wong utilized PRF in experimental models to encourage meniscus chondroblast proliferation (Wong *et al*., 2017). Dermal fibroblast migration and activation, which increased collagen synthesis in skin subjected to PRF therapy, have been reported in dermatology and plastic surgery (Desai *et al*., 2013; Crisci *et al*., 2018).

2-9 Repair of skeletal muscle pathobiology

Mesh integration, biology: After the mesh is implanted, a series of extremely complex processes occur, signaling the start of the healing process. Understanding the biology of mesh integration necessitates a thorough examination of inflammation and its impact on wound healing (Bendavid *et al.*, 2001) when a

new material enters the body, it causes one of three typical reactions: (1) destruction or lysis, (2) integration or tolerance, or (3) rejection (Baylón *et al*., 2017). When no biocompatible materials are introduced into the body, the immune system attempts to destroy or reject them because they are perceived as foreign items (Carnicer-Lombarte *et al*., 2021).

After the implant is certified biocompatible, a four-stage integration procedure begins.

2-9-1 First stage: The Acute Inflammation:

Protein coagulation around the prosthetic implant triggers the initial biological reaction at the injured site (Anderson, *et al*., 2008).The coagulum is made up of albumin, fibrinogen, plasminogen, complement, and immunoglobulins (Judex, and Mueller, 2005).

The synthesis of factors C3a and C5a (chemotactic factors for inflammatory cells), to which platelets attach, causes an ordered movement of macrophages, fibroblasts, smooth muscle cells, and polymorphonucleocytes (PMNs) to the site of the lesion. These elements stimulate both the conventional and alternative complement pathways. (Janeway *et al*., 2001). Chemotactic function is defined as "movement of cells towards a preferred migratory location driven by chemical stimulation." In the acute phase of inflammation, migrating PMNs phagocytose microorganisms and necrotic material. When worn-out PMNs breakdown and release their cytoplasmic and granular contents close to the mesh, an additional inflammatory response may occur (Wang 2009). Chronic inflammation may emerge from this illness if the initial inflammatory response is unable to remove the source of the injury and restore normal physiology to the affected tissue.

2-9-2 The second chronic inflammation:

Monocytes that had migrated to the site of the wound earlier become macrophages at this stage. Other key cellular elements, such as plasma cells and lymphocytes, also actively contribute to the advanced inflammatory response in addition to macrophages. Macrophages begin the phagocytosis of dead cells, necrotic tissue, and devour foreign materials in order to clear the way for the colonization of fibroblasts (Hirayama *et al*., 2017).

2-9-3 Third stage: Foreign Body Reaction:

This type of persistent inflammation is brought on by a biomaterial or implanted medical device. When there are big, indigestible foreign bodies present, macrophages combine to form a foreign body giant cell an effort to enclose the foreign matter in an epithelioid granuloma (Anderson *et al*., 2008). According to the nature, form, and structure of the implanted material, different levels of foreign body giant cells, fibroblasts, and angiogenesis formation are produced during the complicated defense response known as the foreign body reaction (Anderson *et al*., 2008).

2-9-4 Fourth stage: Scar Formation:

In this stage, fibroblasts and other cell lineages replace the damaged tissue to create the extracellular matrix (EMC) and the scar. Persistent inflammation and the severity of the initial damage can have an impact on how well a wound heals and how quickly scars form (Guillamat-Prats 2021). The cells that mediate the process of wound healing are called fibroblasts. Two to five days following surgery, usually after the acute inflammatory reaction has subsided, these cells move into the area of the wound. At the site of the wound, fibroblasts multiply and peak after one to two

weeks. Extracellular matrix (ECM) with collagen synthesis is the primary role of fibroblasts in the regeneration of connective tissue. The collagen matrix, which is deposited by fibroblasts together with local GFs, plays a role in the regulation of inflammation, angiogenesis, and connective tissue regeneration within the EMC (Rodrigues *et al*., 2019).

2-10 Growth Factors (GFs)

Growth factors are soluble signaling chemicals that bind specifically to target cells' transmembrane receptors to regulate biological responses. When growth factors are incorporated into a cell-scaffold architecture, tissue regeneration can be assisted more than when growth factors are not used. Significant progress has been made in abdominal wall reconstruction in recent years. Although the introduction of newer prostheses has improved outcomes, the elimination of mesh-related morbidity remains a challenge. It is thought that host foreign body reaction to prosthesis plays a role crucial role in the biology of these complications, comprehension of the molecular mechanisms underlying mesh-Tissue interactions may be important in future therapies. It appears that increasing biocompatibility of both synthetic and natural materials Prosthesis and biologic scaffolds may be the primary avenues for improved outcomes. Wound healing effectors, with a focus on how their modulation might improve tissue remodeling and mesh integration outcomes, Cytokines and growth factors are important in cell communication. Unlike hormones, cytokines are not stored in glands as preformed molecules but are rapidly synthesized and secreted by various cells, usually after stimulation. Furthermore, cytokines act on a variety of target cells (pleiotropism) and frequently influence the action of other cytokines in an additive, synergistic, or antagonistic manner. Aside from their pleiotropic effects, cytokine actions are frequently redundant—that is, several different cytokines can achieve similar biological responses. (Zhang and An 2007).

Major Cytokines and Growth Factors Related to Wound Healing with their Respective Roles

2-10-1 Interleukins (ILs)

A class of glycoproteins produced by leucocytes for regulating immune responses important members of the cytokine family, are made up of a diverse set of molecules that include a variety of immune mediators that contribute to the immunological responses of many cells and tissues. ILs are immune-glycoproteins that directly contribute to the growth, activation, adhesion, differentiation, migration, proliferation, and maturation of immune cells; and, as a result, they are involved in the body's pro and anti-inflammatory responses via interactions with a variety of receptors. Because of the importance of the immune system in various organisms, the genes encoding immune elements such as ILs have been extensively studied. According to the findings of recent studies, genes related to the immune system evolve at a constant rate (Behzadi *et al*., 2022).

Interleukin-6 (IL-6) is an inflammatory cytokine that is highly elevated in the majority, if not all, inflammatory states. IL-6 causes cell type-specific responses and acts on target cells via an interleukin-6 receptor (IL-6R),which, in conjunction with IL-6, binds to and induces dimerization of a second IL-6 also binds to the soluble IL-6R subunit, gp130, and this complex is formed. Regardless of IL-6R expression interacts with gp130 this enables cells to not express IL-6R and thus would be insensitive to IL-6 in order to respond to it created L-gp130, a constitutively active version of gp130, by crossing mice with any Cre-recombinase, the L-gp130 locus can be activated in a cell-autonomous manner (Rose-John 2022).

2-10-2 Vascular endothelial growth factor VEGF

Is a potent angiogenic factor and was first described as an essential growth factor for vascular endothelial cells angiogenesis is the formation of new blood vessels from pre-existing vessels, and it is thought to be important in wound healing and prosthetic integration. (Johnson and Wilgus 2014). VEGF is one of the most important pro-angiogenic factors. It is found in high concentrations in wound fluids, and its lack of expression results in wound healing defects (Szondi *et al*., 2021). Increased VEGF expression in the endothelium of microvasculature is associated not only with endothelial proliferation, which leads to increased vessel population size, but also with increased permeability, which results in provisional ECM secretion required for angiogenesis (Senger and Davis 2011) Hypoxia is a major inducer of VEGF release, causing cells to express hypoxia-induced factor (HIF). HIF promotes VEGF expression in monocytes, fibroblasts, and endothelial cells. As a result, a strong chemotactic and proliferative effect is produced (Beamer, *et al*., 2010). VEGF is another active cytokine involved in the FBR. Platelets release VEGF in response to tissue injury to promote monocyte chemotaxis and colony formation by granulocyte-macrophage progenitor cells (Sadava *et al*., 2013) Given that VEGF is also a potent chemoattractant of inflammatory cells, continuous VEGF release may prolong the inflammatory response. As a result, VEGF expression around Implants may affect the extent and prognosis of the FBR. Overall, VEGF's central role in angiogenesis is dependent on its ability to regulate multiple endothelial functions. VEGF has the ability to initiate and integrate a network of signaling pathways, making it likely that it is yet another powerful signaling molecule target for translational research (Shibuya 2011).

The most significant GFs involved in mesh integration and tissue regeneration are Growth factor produced from platelets, Proliferation of fibroblasts

and smooth muscle cells is aided by PDGF A-B. A number of cells, including endothelium, smooth muscle, and fibroblast cells, release the fibroblast growth factor FGF-2, which is a strong activator of smooth muscle, endothelial, and fibroblast cells (Everts *et al*., 2023).

TGF, a type of growth factor, is secreted by a variety of cells, including macrophages and PMNs. TGF stimulates monocyte activation and fibroblast formation. Endothelial cells respond strongly to insulin-like growth factor (IGF), which is produced by platelets and fibroblasts. Dermatologic growth factor EGF, which is produced by platelets and macrophages, stimulates the synthesis of extracellular matrix and collagen, which is crucial for the healing of hernias.

The local blood supply is increased locally by new blood vessels that are generated at the injury site by VEGF (Johnson and Wilgus 2014; Veith *et al*., 2018) the primary purpose of fibroblasts is:

Fibroblastic activity peaks about two weeks following surgery, frequently on the eighth day for intraperitoneal access and on the tenth day for extraperitoneal access. The optimal density of fibroblasts, required for the effective integration of the mesh, is attained around two weeks after surgery (Elango *et al*., 2017).

Collagen types I, II, and III, which make up the majority of connective tissue's biomechanical structure, is strong and acts as a scaffold. The best connective tissue synthesis results from a typical fibroblastic biological reaction. Frail, primarily immature collagen type III is produced by fibroblasts and expelled there in a monomeric form, where it polymerizes into an insoluble helical shape. For the first 21 days or so, a fragile collagen network is generated before the ratio of collagen types III and I changes. Collagen type I, which is more robust and persistent, emerges when collagen type III declines. Progressive gains in mechanical strength are seen

up to six months following surgery (Elango *et al*., 2017). As a result, the collagen ratio type I/III and its role in the formation of the ECM have a substantial impact on the quality of connective tissue. Reduced tensile strength and mechanical stability are the results of a changed Type I/III collagen ratio. Therefore, changes in collagen subtypes are crucial to the pathophysiology of mesh integration and hernia repair (Bringman *et al*., 2010; Monika *et al*., 2022). Recent research suggests that the changed ratio of collagen subtypes may be caused by enzymes such matrix metallo-proteinases (MMPs) and the absence of their inhibitors tissue inhibitors of metaloproteinase (TIMPS). Patients with direct inguinal hernias frequently have this alteration in the transversals fascia (Bellón *et al*., 2021). These enzymes' primary job is to work on specific types of collagen and elastin to breakdown and speed up the turnover of the extracellular matrix (EMC). The main matrix enzymes in charge of type I, type II, and type III collagen turnover are MMP-1 and MMP-13 (Nizar *et al*., 2021). Therefore, the derangement of the type I/III collagen ratio may be caused by changes in MMP-1 and MMP-13 protein expression (Elango *et al*., 2017).

In the wound area, excessive fibroblasts and related hyperactivity will extend the inflammatory phase, which will increase fibrosis. This will hinder the best collagen synthesis and, consequently, the integration of the prosthesis. Prolonged inflammation may compromise the mesh's ability to integrate, which may then cause the mesh to compress and shrink, eventually leading to fibrosis, adhesions, and fistulas. Rejection of the prosthesis may result from this (Kalaba *et al*., 2016).

Chapter Three

Materials and Methods

3-1 Experimental Animals

In the current study, (36) of adult Iranian rams, which were clinically healthy, weighing (45±0.7 kg) and aged (16±0.8 months) were included in this study. All animals were clinically examined and housed under the same management conditions and accommodations in animal's house of the College of Veterinary Medicine/ University of Mosul, for two weeks before starting of the experiment. They were injected subcutaneously with enterotoxaemia vaccine (Zoetis, USA) at a dose of 1ml/ animal, and dewormed with Ivermectin (KEPRO, Holland) at a dose of 0.2 mg/Kg B.W/SC. The animals were numbered and divided according to the experimental design.

3-2 Ethical Approve

The research was approved by Ethics Committee of Faculty of the College of Veterinary Medicine Medicine/ Mosul University No UM.VET.2021.055

3-3 Experimental Design

A protocol of sedation and local anesthesia included (xylazine HCL (Interchem, Holland0.1 (mg \kg B.W/ IV. Lidocaine HCL (Johnlee pharmaceuticals, India) 3.4mg \kg B.W (Greene and Thurmon 1988) were suggested in all experimental animals to perform surgical operation with minimum degree of pain. An experimental ventro-lateral hernias 10cm diameter were created at the right abdominal wall of all experimental animals (Al-ebadi and Al-Bayati 2019). One month post inducing hernia, the rams were randomly allocated into three equal

groups (12 of each group), the induced hernia in all experimental animals repaired as followings:

G1: In this group, hernias were treated with implantation of synthetic polypropylene mesh alone and consider as control group.

G2: hernias were treated with the implantation of polypropylene mesh and supplemented with adding 5 ml Aloe Vera gel (which prepared immediately as fresh juicy gel from Aloe Vera leaves).

G3: which was treated with polypropylene mesh and supported with PRF which prepared according to Mohan *et al.*, (2019).

The macroscopically and histopathological and immunohistochemistry examinations were performed at 7, 15, 30, and 45 days after treatment.

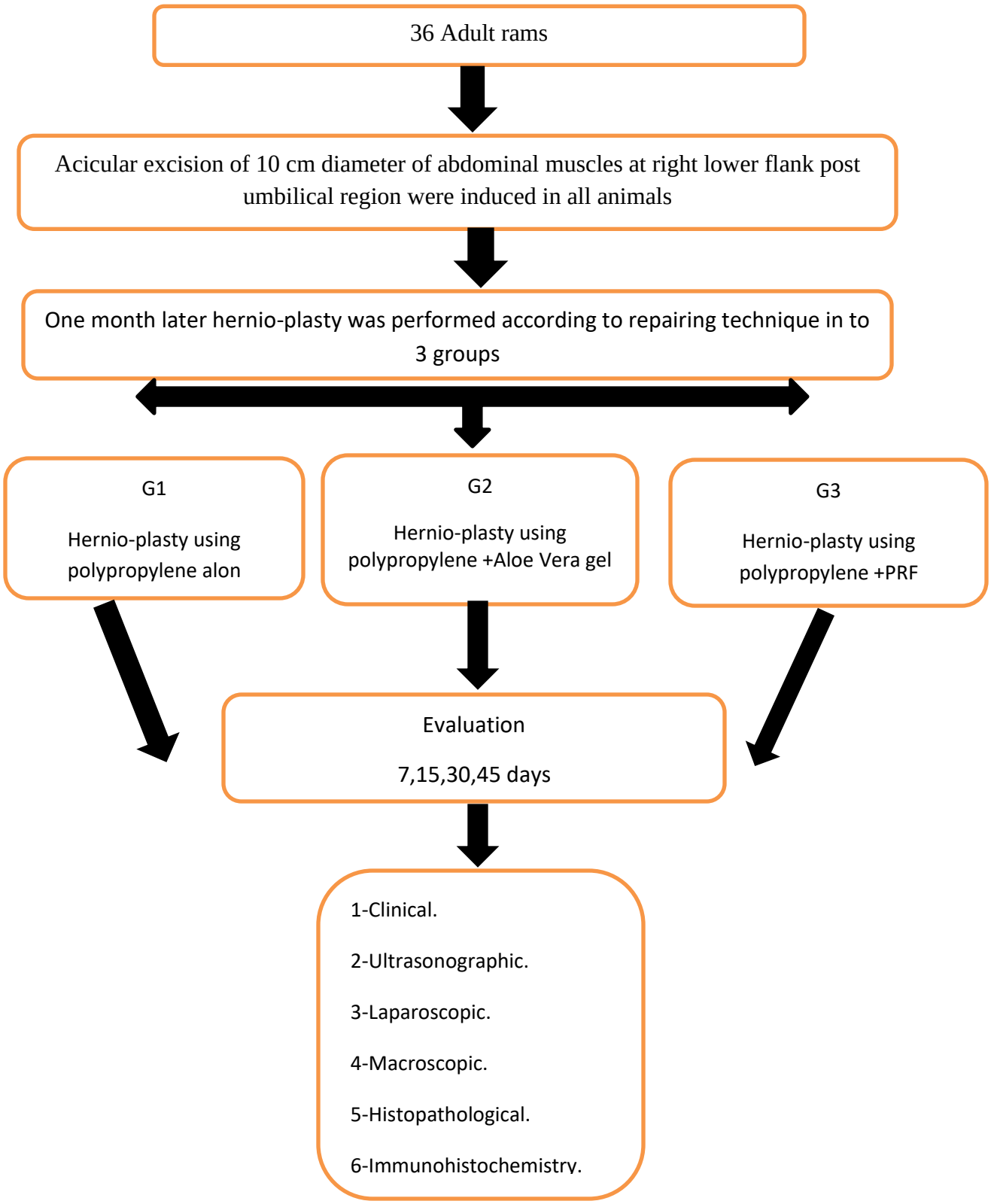

Figure 3-1: illustration shows the experimental design of the study

3-4 Inducing of Ventro-Lateral Abdominal Wall Hernia

Food withholds for 24 hours and water for 12 hours in all expermented animals pre-inducing of hernias. The animals were injected intramuscularly with penicillin streptomycin (Interchemie, Holland) 12 hours preoperational at a dose of 10000 IU and 10 mg/kg B.W. respectively. Under the effect of sedation by intravenous injection of 2% xylazine hydrochloride (Interchemie, Holland) at a dose of 0.1 mg/kg B. Wt.(Emon 2022).The animal lay down at lateral recumbency, the right lower flank post-umbilical region of all animals was prepared for aseptic surgical condition, and the surgical site was then prepared (Figure 3-2). A protocol of local infiltration through an inverted (L) shape by using 2% lidocaine hydrochloride (Johnlee Pharmaceuticals, India) at a dose of 3-4 mg/kg B.w. (Simpson *et al.*, 2022). The skin and subcutaneous fascia were incised in a vertical, straight line for 10 cm, after which the skin and fascia abruptly detached from the abdominal wall muscles. These muscles were elliptically resected to a full thickness of 10 cm without (Figure 3-3) penetration the peritoneum layer, the subcutaneous tissue and skin closed by interrupting horizontal mattress (Silk No.1). (Figure 3-4).

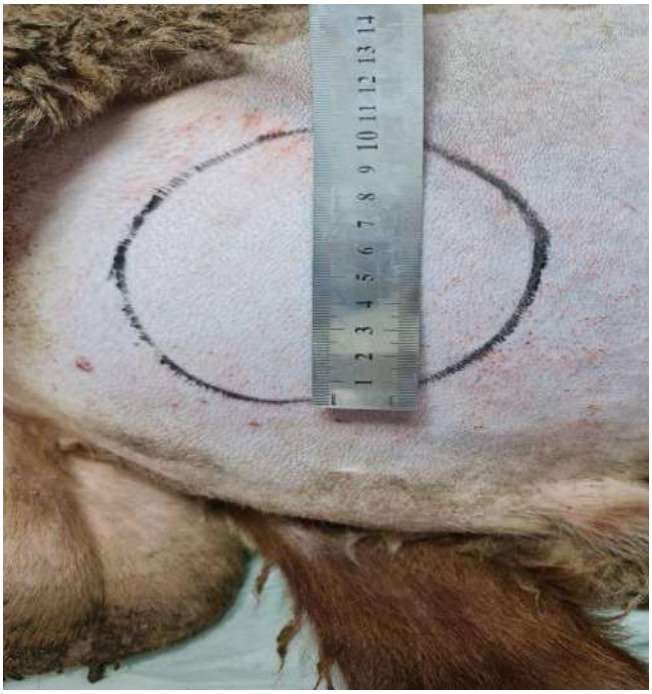

Figure 3-2: Photographic picture of ram Shows preparation of surgical site with determine the size of removal muscles

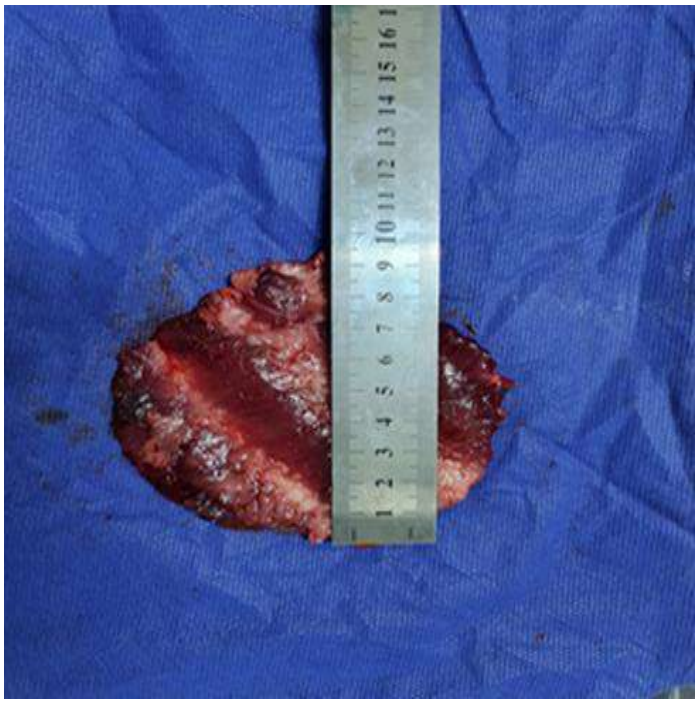

Figure 3-3: Photographic picture Shows 10 cm abdominal wall muscles which excised

Figure 3-4: Photographic picture of ram after 30 days post-surgery show the induced ventrolateral hernia.

3-5 Aloe Vera Gel preparation

One of the outer leaves at the plant's base was cut off before a fresh Aloe Vera leaf was plucked. It was then thoroughly cleaned, free of any dirt, and set upright in a cup or bowl for ten to fifteen minutes. This enables the yellow resin to come loose from the leaf. The latex found in the resin has the potential to irritate. Any remaining resin on the paper was washed off after the resin had fully dried, and the thick layer was removed using a small knife or vegetable peeler. When the leaf is removed, the pure natural Aloe Vera gel is visible. The gel was then scooped and added to the blender with a small spatula. It only needed to be a matter of seconds to blend the gel until it was liquid and foamy. The gel becomes ready to use application in different purposes (pattnaik *et al*., 2022).

Figure 3-5: photographic image show preparation of Aloe Vera gel and its final apperance.

3-6 Platelet rich Fibrin (PRF) Preparation

The autogenous platelet-rich fibrin was made just prior to surgery by taking 30 ml of whole blood from the own surgically operated animal's jugular vein and centrifuging for 10 minutes at 3000 rpm without the use of any anticoagulants. After centrifugation, a sterile tube with three distinct layers was obtained. The middle layer was made up of fibrin-rich platelets that had been separated from the bottom layer of red blood cells. The top layer was made up of plasma with poor platelets (Raaj *et al.,* 2015).

3-7 Treatments of Hernia

Thirty days post inducing of hernia and after making sure that the hernia has occurred and verifying the completeness of the contents of the hernia by clinical examination, hernias were identified clinically by the presence of a hernia ring, content, and sac. The operative animals were prepared aseptically for hernioplasty. Penicillin and streptomycin were intramuscularly injected as a prophylactic treatment 12 hours prior treatment as in case of inducing hernias animals submitted to same protocol of sedation and local anesthesia, as previously mentioned. 10 cm of skin were vertically incised and straightly, parallel to the previous skin incision. Then used gentle, blunt dissections of the underlying tissues to break up adhesions to determine the boundaries of the hernia ring. Pushing the hernia's contents into the abdominal cavity and reshaping the hernia ring's border. After that, the hernia was repaired using polypropylene mesh (30×30cm) (Betatech®)-Turkey, with modified two layers sub-lay technique (Figure 3-6). According to this modified technique The polypropylene mesh firmly fixed at the borders of the muscular layers of the abdominal wall using a U-shaped suturing technique, 2 cm away from the hernia ring's edges, making use of synthetic, non-absorbable suture materials

(polypropylene No.1) Sharp incisions were made to remove the access skin and subcutaneous tissue, and then silk No. 1 was used to oppose the horizontal mattress suture pattern in the first group (1) the second group (2) Aloe Vera gel 5 ml added by spreading over the mesh the 3ed group (3) adding about 5 ml of autogenous PRF.

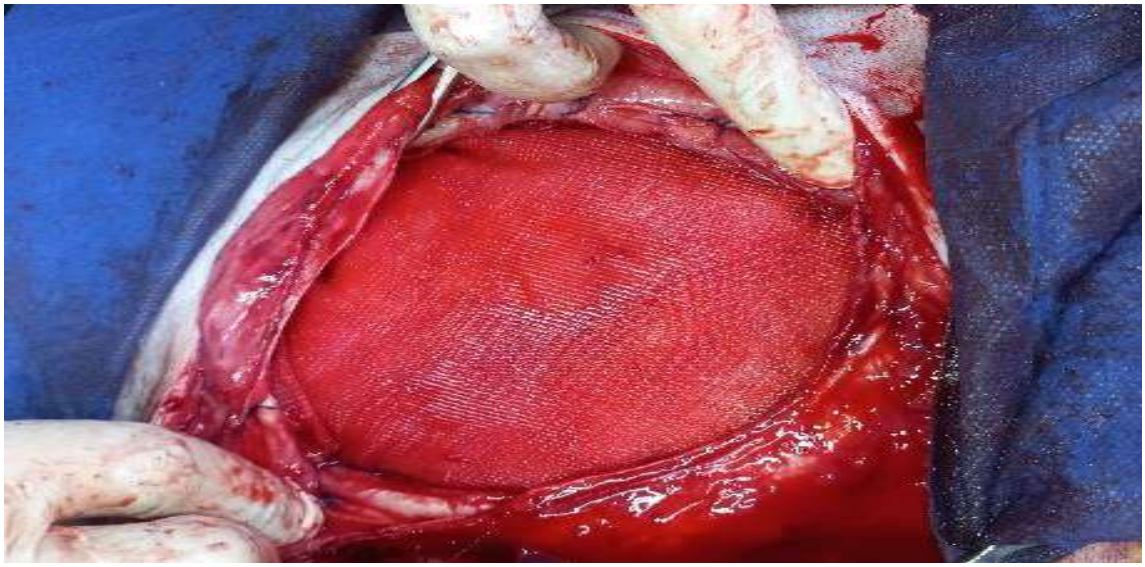

Figure 3-6: photographic image Shows modified sub-lay mesh fixation

3-8 Post-operative Care

After the surgery, care was followed to monitor the animal, antibiotics and dressing were used by using wound spray OTC spray (Norobrook. ERLANDA) twice a day for five days .Subjecting the animals to a balanced diet and restrict the animals unnecessary movement to avoid self-trauma and wound opening and dehiscence. Penicillin- streptomycin at a dose of 10000 IU and 10 mg/kg B.W. Respectively for 5 days post-operation was used intramuscularly as Anti-inflammatory agent and analgesics Dipyrone (Metamizole) (SPI) 1ml\10 kg BW was given for 3 days post operation. The stitches were removed after 8 days.

3-9 Assessments

Clinical, ultrasonographical, laparoscopic, macroscopical, histopathological and immunohistochemistry investigations were used at 7th, 15th, 30th and 45th days post- hernioplasty. Following repairing of hernia, all animals were daily inspected clinically along first week and then after (15, 30, and 45) days post-surgery, the clinical inspection including presence of seroma, recurrence of hernia, inflammatory signs. The ultra-sonographic investigations were done by using (Kaixin Kx5100vet 3,5microconvex probe Keebromed USA) at deferent period post treatment at (7, 15, 30, and 45 days). The laparoscopic inspection was done by using camera system ((Karl Storz Endoscopy America, Inc., Germany) at deferent period post-surgery at (7, 15, 30, and 45 days) to confirm diagnosis and to determine the presence and degree of adhesion.

3-9-1 Clinical Evaluation

The animals were observed daily inspection whole along the period of study to record general health, behavior and alertness and activity. Post-inducing of hernias, the clinical examination included any swelling, presence of hernia components, any complications as seroma, inflammatory reactions or abnormal discharge from the site of operation until repairing hernias. Post-treatment of hernias, clinical examination was also performed daily, to evaluate the presence of local or systemic complications.

3-9-2 Ultrasonographical investigation

Ultrasonographic investigation was acheived using (Kaixin Kx5100vet 3,5microconvex probe or 5.5MHZ Keebromed, USA) images was taking pre-inducing hernia's and considers as control reding then are taking at 7th, 15th , 30th

and 45 post hernioplasty to track the healing process progressing of abdominal wall hernias. The animal positioned on surgical table at lateral recumbence position. The site of ultrasound investigation was prepared aseptically. The procedure done using the 5.5 MHz curvilinear multifrequency. From the healthy wall towards the hernioplasty, the transducer was rotated either craniocaudally or dorsoventrally. The alterations at the implantation sites were described using the terms anechoic, hypoechoic, and hyperechoic (Hummadi and AL-Asadi 2011).

3-9-3 Laparoscopic Evaluation

Laparoscopic investigations were performed in aseptic condition using cameral system device (Karl Storz Endoscopy America, Inc., Germany).All experimental animals were fasted 24 hours pre-laparoscopic investigation, the site of introducing laparoscopic tools was prepared routinely and the animals undergoing protocol of sedation and local anesthesia including xylazine 0, 1 mg/kg BW along with lidocaine 2%/3-4 mg/kg BW. Animal positioned in dorsal recumbency (supine position). The tools and equipment required to carry out laparoscopic procedures were used. Five centimeters cranial to the umbilicus, a small cutaneous incision was made in the midline. It was done using a Verses needle. A 15 mmHg-pressure pneumoperitoneum was produced. (Al-Wataar *et al.,* 2009). The Verses needle was taken out after the abdomen had become swollen. The needle's insufflator pipe was separated from it and connected to a trocar that was positioned nearby. Through the identical trocar, an optic was inserted through the same trocar. Subsequently, the entire abdominal and abdominal cavity was examined for any abnormalities as abnormal fluid in the abdominal or profuse adhesion or any inflammatory reactions (Piątek *et al*., 2015).

3-9-4 Macroscopical Evaluation

Macroscopic examinations were performed at 7th, 15th, 30th, and 45th days post treatment, a visual inspection of the implantation area was carried out under sedation and local anesthesia. A vertical skin incision was made cranial to the hernia in 3 rams per period, site to expose the implantation site. The flap, which included the skin and subcutaneous tissue, was then reflected-up, exposing and exposing the mesh site. Gross examination was performed to look for signs of heavy bleeding, implant degradation, integration of the implant into the surrounding tissues, closure of the hernia opening, infection, or mesh rejection, adhesion. (Gumaa and AL-Bayati 2021).

3-9-5 Histopathological Evaluation

Samples were collected for the histopathological and immunohistochemistry examination. (3 samples each period for each groups) The cranial edge of the implantation site and the margin of the implantation site with 1 cm of surrounding tissue were sampled. The samples were immediately fixed in 10% buffered formalin solution, embedded in paraffin, sectioned longitudinally to create 5-7 m thick sections, and stained with hematoxylin and eosin (H&E) (Calvi *et al.*, 2014). In the course of the study, a scoring system was used to evaluate the analysis of the histopathological scores of healing progression in the implantation sites. Within the scoring system, more favorable outcomes are represented with regard to remodeling, as demonstrated by cellular infiltration, cell types, host ECM deposition, scaffold degradation, fibrous encapsulation, and neovascularization.

3-10 Tissue processing and sectioning

After tissue collection, the samples were fixed in 10% neutral buffered formalin (prepared by adding 10 ml of 37-40% formaldehyde to 90 ml of distilled water containing 4 grams of sodium phosphate monobasic salt and 6.2 grams of sodium phosphate dibasic salt) to start the tissue fixation, and this stage lasts at least 72 hours, later these samples were washed in running tap water for one hour, then processed to be embedded in paraffin wax (Luna 1968). The samples were later carried in tissue cassettes and labeled with each group and animal code, and then these samples were dehydrated to remove the water from tissues using ethyl alcohol; this process starts with 70% ethyl alcohol overnight, then 80% ethyl alcohol for one hour, 90% ethyl alcohol for one hour at two changes, then the samples transferred to absolute alcohol for one hour at two changes (Luna, 1968). At this stage, the water was excluded from tissue and ready to be cleared with xylene, which was used as pure as its supplied for thirty minutes at two changes, with visual examination until the tissue had a clear yellow to brown gelatinous appearance to complete the clearing process and at this stage, the tissue was ready to be infiltrated with paraffin wax (Luna, 1968). After the clearing was complete, the samples were transferred to hot paraffin wax at 55-58ºC for one hour at three changes (the first changes should have 50% xylene and 50% paraffin wax, the second changes should have 25% xylene and 75% paraffin wax, the third changes should be 100% of hot paraffin wax) at the end of this stage the samples should have a solid, firm and natural tissue color which mean the tissue was completely infiltrated with paraffin wax (Luna, 1968). The tissue samples are then embedded in paraffin wax by using paraffin mould where the mould is filled with hot paraffin wax, and the tissue sample is localized in the center of the mould and filled mould to the cassettes, then left to be cooled at the room temperature (Luna, 1968). The paraffin block sectioning using rotary

microtome at 4-6 µm then transferred to the floatation water bath, and lifted using labeled clean glass slide, and dried at room temperature for 24 hours, then slide put on a hot plate to complete drying for one hour at 55-60ºC, the slide was ready to stain (Luna, 1968).

3-10-1 Harris hematoxylin and alcoholic eosin

The glass slides were stained with routine Harris hematoxylin and alcoholic eosin stain using the standard protocol described by Luna (1968):

1- The paraffin wax was removed using xylene for three changes, ten minutes each.

2- The slides rehydrated by ethyl alcohol, 100%, 90%, 80% 70%, two changes, five minutes each.

3- The slides floated with tap water for 10 minutes to complete the rehydration.

4- The slides were stained with Harris hematoxylin for ten minutes.

5- Slides were washed with tap water and blue using saturated lithium carbonate solution.

6- Slides washed in running tap water to develop the sky blue color.

7- Slides rinsed with 90% ethyl alcohol for one minute.

8- Slides stained with alcoholic yellow eosin for two minutes.

9- Slides were dehydrated using ethyl alcohol 70%, 80%, 90%, 100% tow changes, five minutes each.

10- Slides cleared in xylene three changes, fifty minutes each.

11- Slides cover with glass slide using DPX tissue mount media.

12- The result of this stain was, the blue color and their shadows stain the basophilic cell element such as the nucleus and nuclear material, while the red and pink color stain the eosinophilic components such as cytoplasm.

3-11 Histological Scoring

The healing process scoring were applied using microscopic examination of the site where mesh implanted materials are applied, this examination were applied in 7, 15, 30 and 45 days after surgical implantation. The histological examination is applied location in which the slides were stained in Harris' hematoxylin and eosin for general observation of healing process, in addition to using immunohistochemical staining using IL-6 and VEGF-A antibodies to help of scoring the bone formations (Luna, 1968).

The histological scoring is used to convert non parametric histological changes into numerical data that can be easily processed statistically to clarify the differences between different groups, in which the main features of normal histological process where taken under investigation, these elements were explained in Table no, 1 (Tabola, *et al.*, 2016), in which the high scoring rank were express optimized healing process:

1- The inflammatory reaction.

2- Formation of granulation tissue.

3- Formation of newly blood vessels.

4- Expression of IHC markers of IL-6.

5- Expression of IHC markers of VEGF-A.

Table no.1: Microscopic scoring criteria that included in current study (Tabola *et al.*, 2016)

Criteria	0+	1+	2+	3+	4+
Inflammatory process	Absent 0 cells/field	Scant 1 to 3 cells/field	Weak 4 to 10 cells/field	Moderate 11 to 25 cells/field	Severe More 25 cells/field
Granulation	Absent 0% (field)	Discrete 1-10% (field)	weak 11-25% (field)	Moderate 25-50% (field)	Sever More 50% (field)
Angiogenesis	Absent 0 (BV/field)	Discrete 1-3 (BV/field)	Moderate 4-10 (BV/field)	Intense 11-25 (BV/field)	Massive More 25 (BV/field)
Fibrosis	Absent 0% (field)	Discrete 1-10% (field)	weak 11-25% (field)	Moderate 25-50% (field)	Sever More 50% (field)
IL-6	Negative - 0 cells/field	Weak ± 1 to 15 cells/field	Positive + 16 to 30 cells/field	Positive ++ 31 to 50 cells/field	Positive +++ More 50 cells/field
VEGF-A	Negative - 0 cells/field	Weak ± 1 to 3 cells/field	Positive + 4 to 10 cells/field	Positive ++ 11 to 25 cells/field	Positive +++ More 25 cells/field

3-13 Immunohistochemistry analysis

Immunohistochemistry was achieved by using the avidin-biotin immunoperoxidase technique. The tissue sections deparaffinized, rehydrated, deactivated then submitted to IHC protocol. Endogenous peroxidase blocked by 3% hydrogen peroxide-methanol solution for 10 min. Washed in PBS at pH 7.4. Blocked by 0.5% goat serum for 30 minutes at room temperature. The slides were incubated with primary antibodies for IL-6 (Post *et al.*, 2016) and EVGF-A (Maae *et al.*, 2011) which is a rabbit polyclonal antibodies at dilution equal to 1:100 (My BioSource, USA) for overnight at 4ºC. Later slides washing with PBS for three times for three minutes each, then incubated with poly-HRP goat anti-rabbit IgG as a secondary antibody at dilution 1:400 (Wuhan Fine Biotech, China) for 30 minutes at 37ºC, then washed with PBS, the stained using Dab system. The slides were counterstained with haematoxylin, rinsed in distal water, dehydrated and cover slipped. Using Image J program, IL-6 and EVGF-A staining was evaluated by find out the density of positive nuclear of cytoplasmic.

3-13 Statistical analysis

Using SPSS version 22.0 to measures the significant differences at $P<0.05$ to compare between different mean for different treatments, in which the One Way ANOVA were used and the Post Hock Test was Duncan's test were used to measures the significances between different groups at $P<0.05$.

Chapter Four

Results

4-1 Post-Operative Observations

Following hernia induction, all study animals underwent clinical and physical examinations, which revealed minor, non-specific secondary health problems as minimal depression, lethargy, decreased animal activity, and decreased appetite. Passed regular feces for the first 48 hours following surgery. Within 3-5 hours of the operation, the site displayed the classic symptoms of inflammation, such as redness, heat, swelling, and pain. These symptoms persisted and peaked 24–48 hours later. The surgical wounds healed without any complications; throughout the periods of follow-up until the hernias were treated, no signs of bleeding or hematoma, infection or stitches abscess were noted. A clear palpable hernia ring with thick, rounded edges and an inverting hernia sac had developed as a reducible ventro-lateral hernia. (Figure 4-1).

Figure (4-1): Photographic image show reducible ventro-lateral hernia palpable ring.

4.1.1 Seroma

Following hernioplasty a seroma developed in the lower region of the surgical site, which was clearly visible as a gradual swelling that resembled a sac between two and five days later.as in (Figure 4-2) the number of animals developed seroma was 3 animals in control group and 2 animals in Aloe Vera group and 1 animal in PRF group and the size, duration and severity was greater in control group then in Aloe Vera group and lesser in PRF group. The seroma that formed gradually subsided during 25-30 days post operation.

Figure (4-2): Photography of ram in control group show seroma at operation site 10 days post treatment

4-1-2 Recurrence

Over the course of the study, no signs of hernia recurrence were seen in any of the experimental animals, and the hernia ring completely vanished in all of the hernias that had been repaired with polypropylene mesh.

4-1-3 Abscess formation

Where it was observed that the abscess was formed in the repair area in three animals from the first group (G1), and the abscess observed in the location of the fold formed by the polypropylene mesh, and the abscess was directly above the mesh in two of the cases, while no abscess was observed in the animals of the two treated groups.

4-2 Ultra-sonographic Assessment

Following hernia induction, abdominal muscle discontinuity and the absence of the normal abdominal wall architecture were visible as in (Figure 4-3).

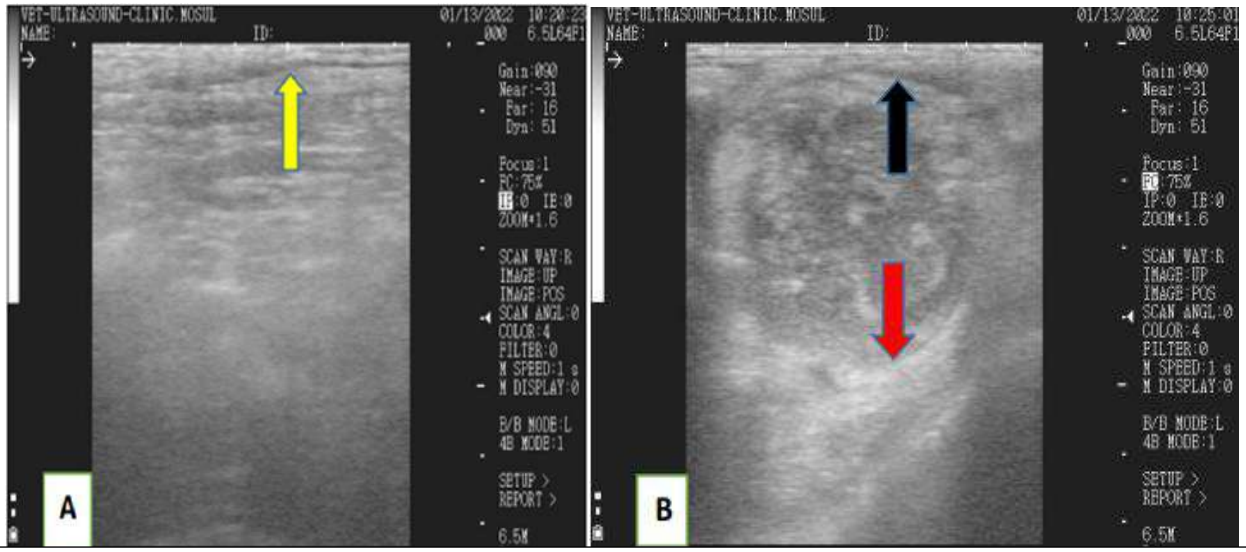

Figure (4-3): Ultrasonographic images (A)pre inducing hernia normal appearance of abdominal wall arrow (B)30th day post-inducing of hernia show disappearing of normal architecture of abdominal wall (black arrow) and formation of hernia ring arrow.

Compared to the normal ultrasonographic images taken prior to the induction of hernias, which appeared as an anechoic area associated with the development of the hernia ring 30 days after induction. All groups were examined after 7, 15, 30 and 45 days after hernioplasty in the lateral lying position.

The results of the ultrasound examination, 7th days after the hernia repair, indicated implanted surgical mesh exhibited in the form of a zigzag line hyper echogenic, with the formation of a layer Hypoechogenic of inflammatory exudate under and above the mesh with Increase thickness of sub-cut and muscle mass (Figure 4-4).

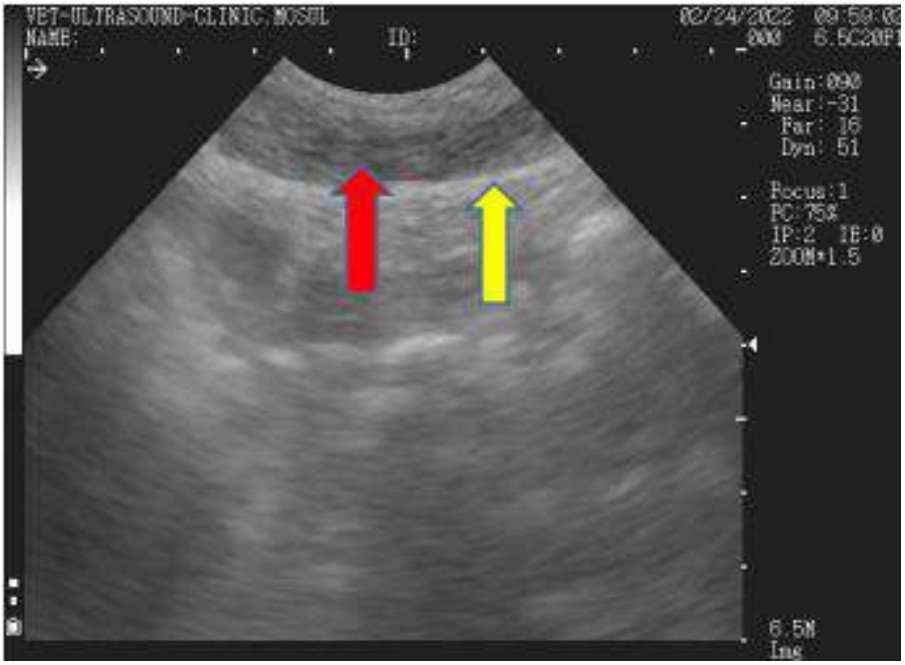

Figure (4-4) Ultra-sonographic image 7days post operation of G1 showing inflammatory exudate arrow and hyperechoic line of mesh arrow.

At 15days post-treatment, the ultra-sonographic images appeared that the exudate fluid started to decrease in the size and there was gradual participation of granulation tissue at the sites of implantation So, the anechoic appearance

at the sites of implantation was replaced gradually by hypoechoic appearance (Figure 4-5).

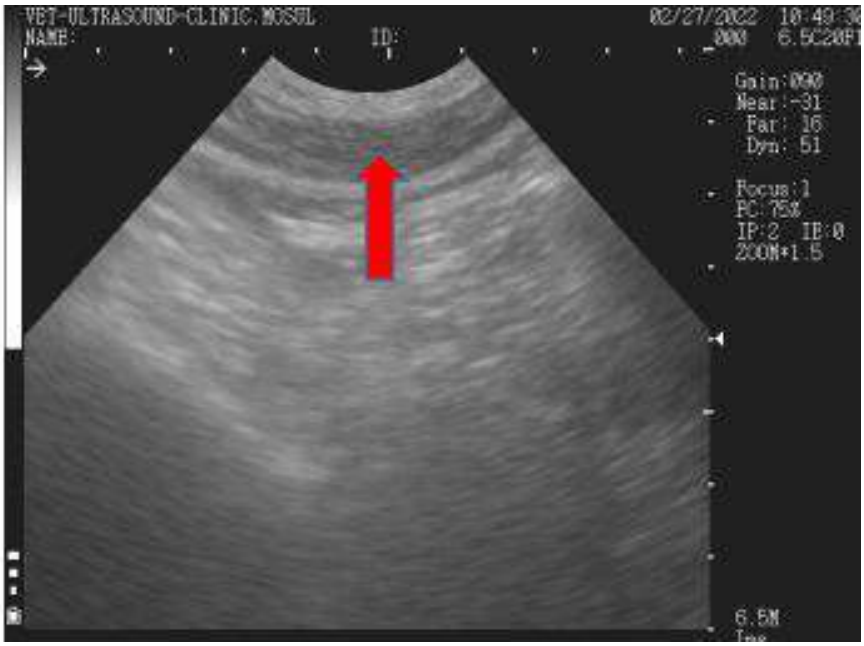

Figure (4-5) Ultra-sonographic image of G1 15 days post operation gradual participation of granulation tissue at the sites of implantation arrow

The most complications seen in control group was seroma which appears as anechoic (hypoechoic) with trabeculae above the hyper echoic line of mesh as in (Fig. 4-5) as well as appearance of granulomatous lesion as in (Figure 4-7). The US indicated presence of abscesses also was seen in this group which appears as an abscess demonstrates, as an irregular border, posterior acoustic enhancement and pusistalsis as in (Figure 4-8).

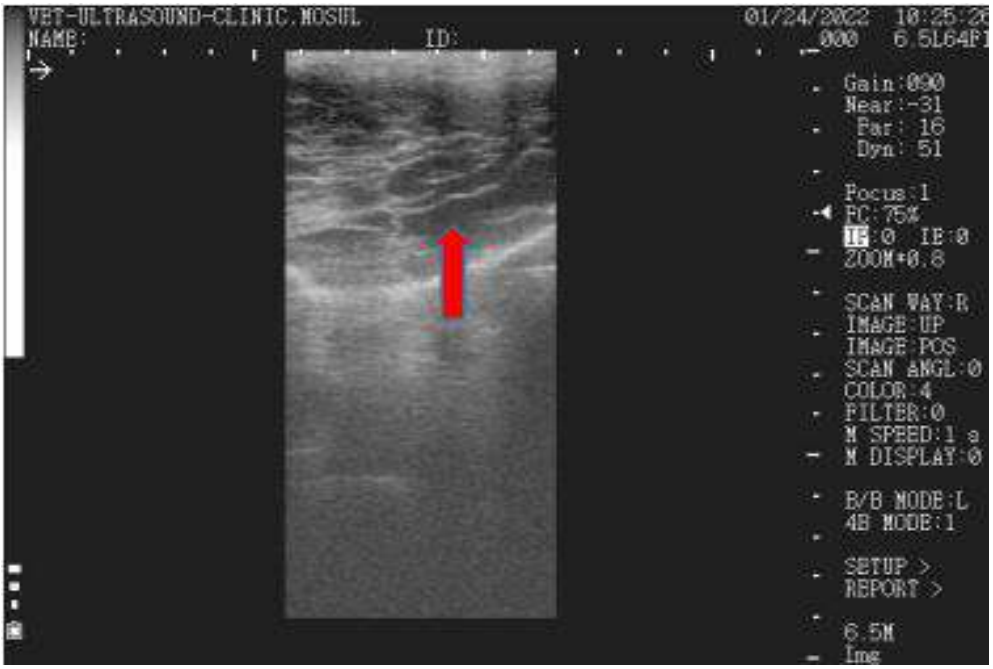

Figure (4-6) Ultra-sonographic image of G1 revels seroma formation 15 days post treatment the anechoic arrow with trabeculae.

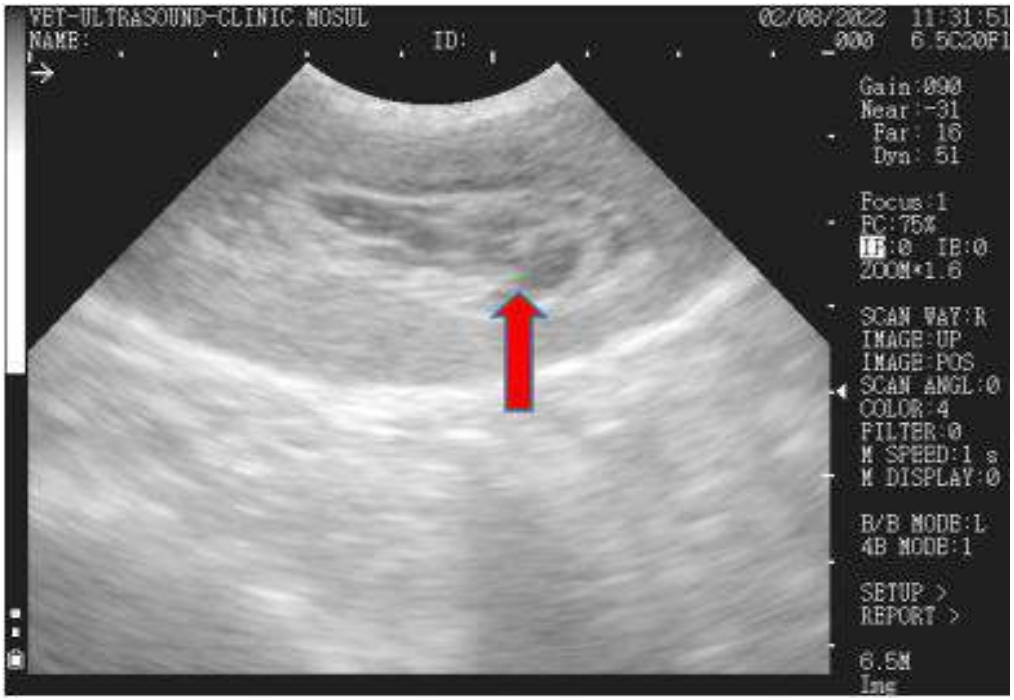

Figure (4-7) ultrasonography image of G1 15 days post operation reveals granulation tissue formation arrow.

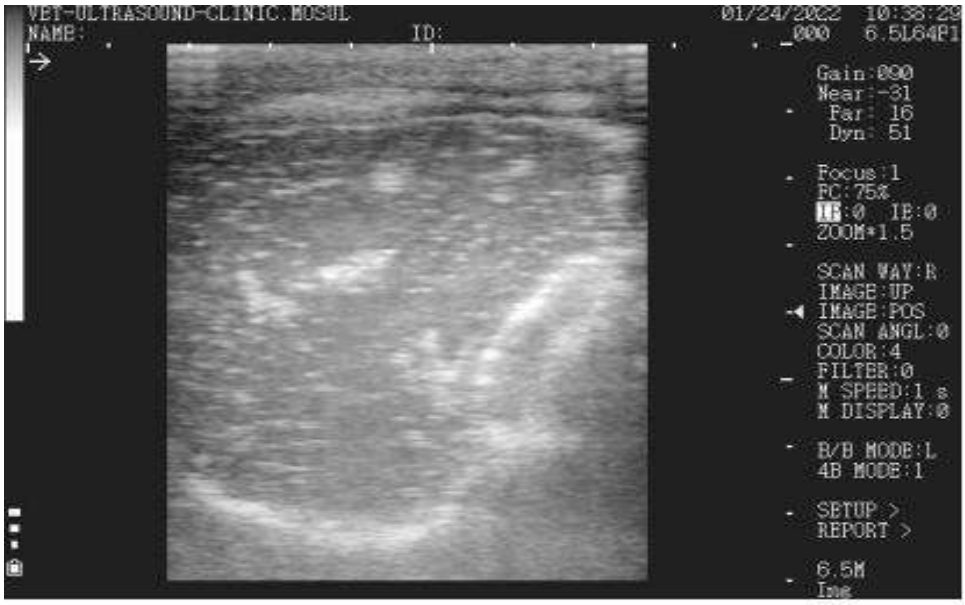

Figure (4-8) ultra-sonographic image of G1 15 days post operation revels abscess formation posterior acoustic enhancement and pusistalsis.

In control group, 30 and 45 days after the hernia repair, an increase in tissue density (increase echogenicity) and a decrease in fluid volume were observed, with the formation of dense layers of fibrous tissue fused with the mesh (Figure 4-9).

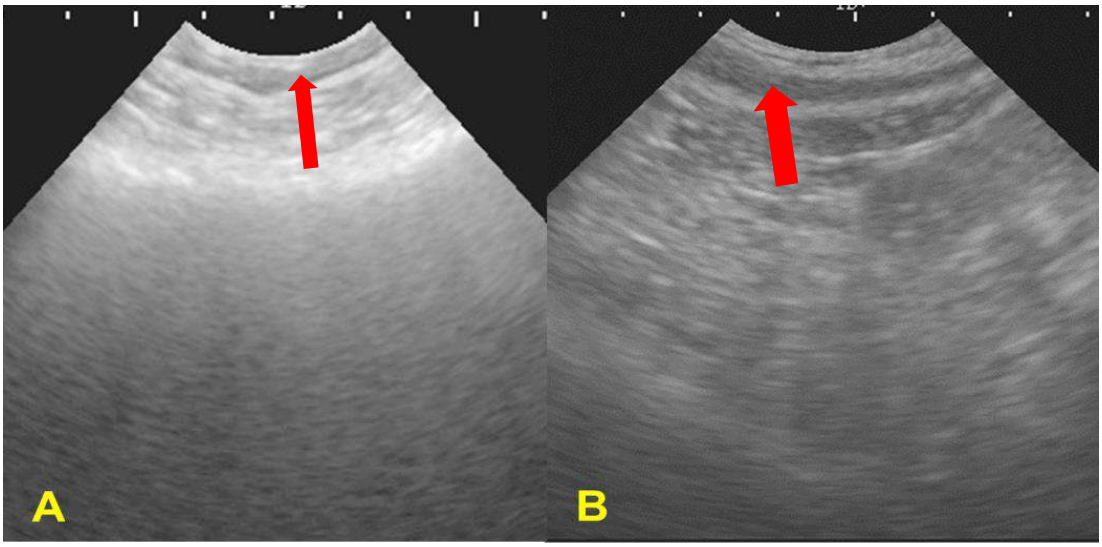

Figure (4-9) Ultrasonographic image (A) 30 days post hernioplasty of G2 gradually deposing of hyper echoic fibrous area (B) Complete healing with absence of hypoechoic inflammatory exudate 30 days post treatment G3 arrow.

The amount of inflammatory exudate was found to be higher in the repair group using a polypropylene mesh and (G 2) when compared to the G3 for the same durations of 7, 15, 30, and 45 days, as shown in the (Figure 4-10).

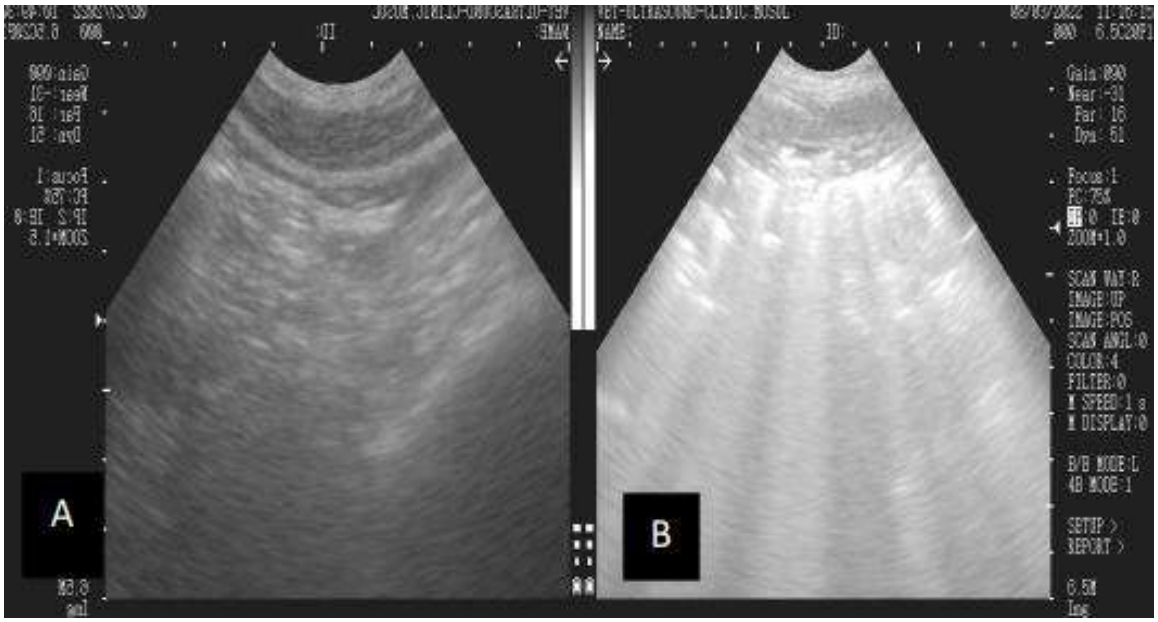

Figure (4-10) Ultasonographic image (A) Hypo-echoic inflammatory exudate 7 days post treatment of Aloe Vera group compering to (B) 7 days of PRF group.

On ultrasound imaging, 30 days after the hernia repair, only one animal in the G3 appeared to have an abscess that was in the subcutaneous area directly above the repair area and was unable to spread to the polypropylene mesh are an abscess appears as a spherical or oblong anechoic or hypoechoic collection containing hyperechoic debris (Figure 4-11).

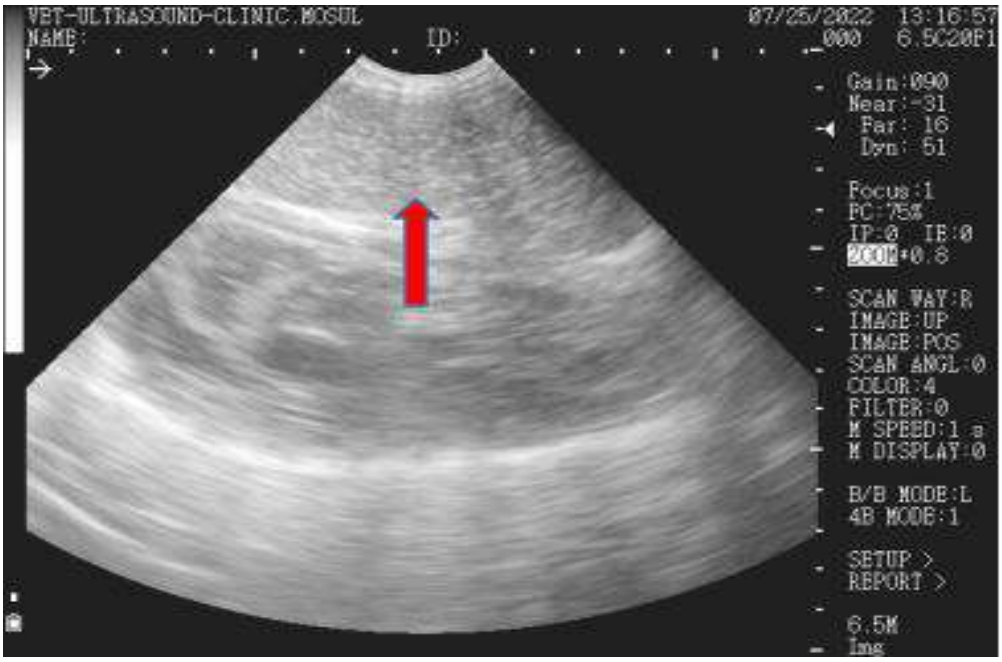

Figure (4-11) Ultra-sonographic image 30 days post-surgery in G3 oblong hypoechoic collection containing hyperechoic debris arrow.

The ultra-sonographic images 45 Days post treatment in all 3groups animal appeared the gradual replacing of anechoic appearance of implantation sites by hypoechoic to echoic appearance. These changes in echogenicity may be due to gradual resolution of exudate fluid and replaced by granulation tissue formation which was more clearly in group B and C than in group A. The echoic to hyperechoic appearance of the implantation sites post-treatment also was more clearly in group 3 than in group 1 and 2 as in (Figure 4-12).

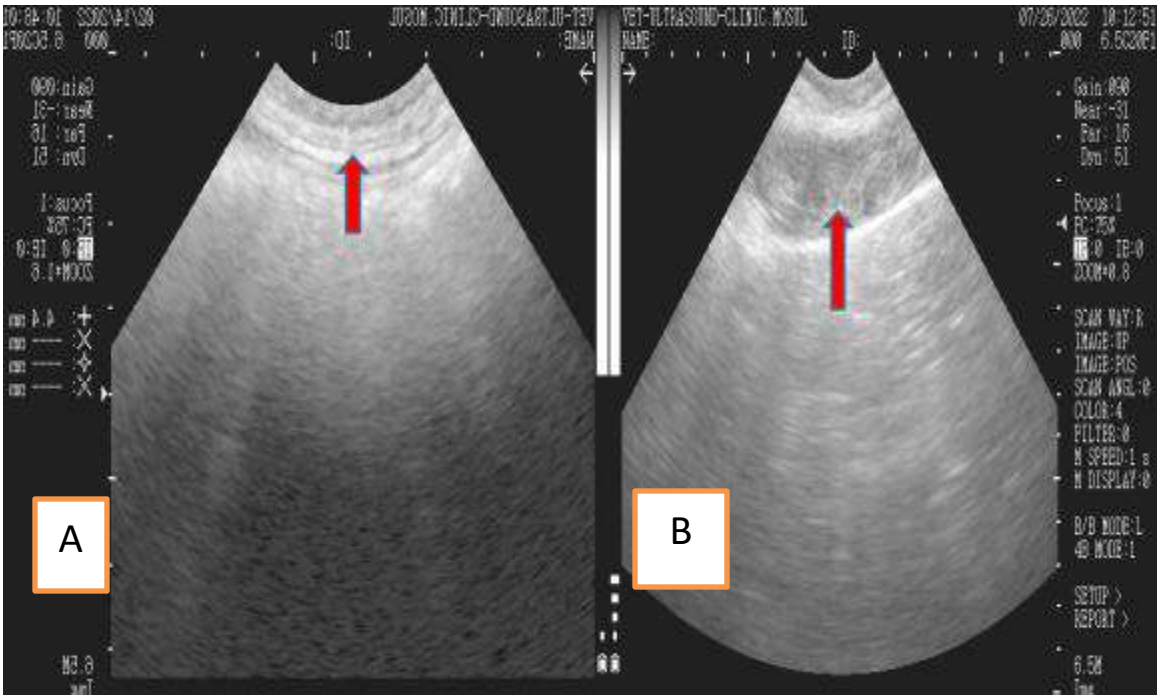

Figure (4-12) Ultrasonographic image 45 days post hernioplasty (A) group 3 (PRF) Comparing to 45days of group 2 Aloe Vera gel (B) echogecity defer above the mesh red row.

4-3 Laparoscopic assessment

In all experimental animals, of thre groups, and for the periods 7, 15, 30, and 45 days after the hernia repair, laparoscopic surgery's assessment of adhesion intensity revealed complete adhesion of the omentum with a polypropylene mesh, as well as adhesion of the suture area. The stability of adhesion increased with the periods, as it was observed where the congestion gradually decreased, also there was no intestinal or other internal organ adhesions (Figure 4-13).

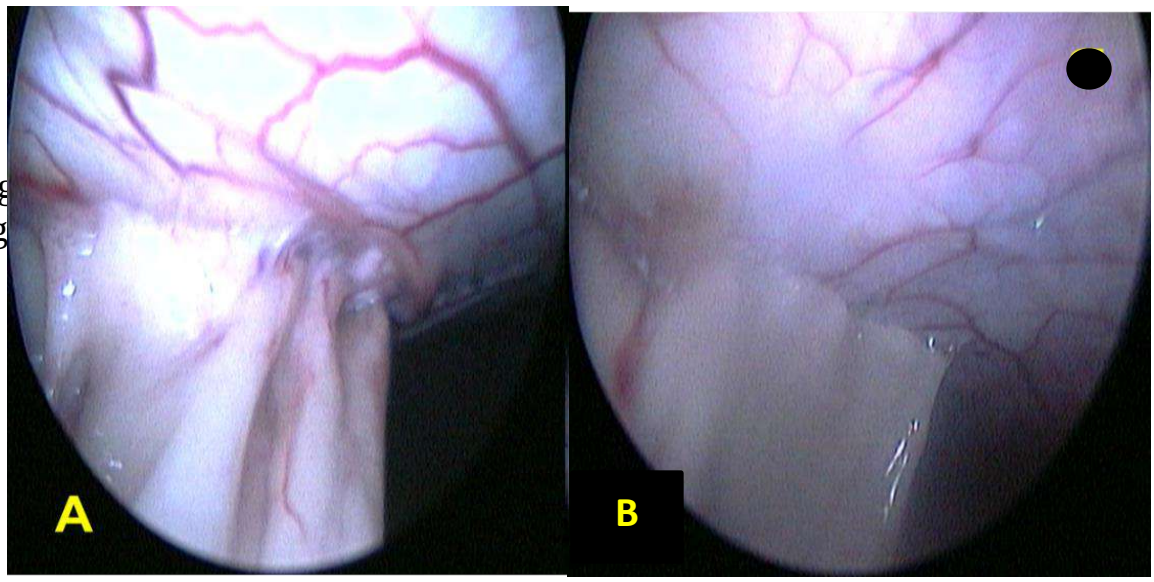

Fig
cong

4-4 Macroscopic Examination

A variation in the size of the hernial sac was noted as well as a variation in the size of the hernial ring as in (Figure 4-14) and (4-15).

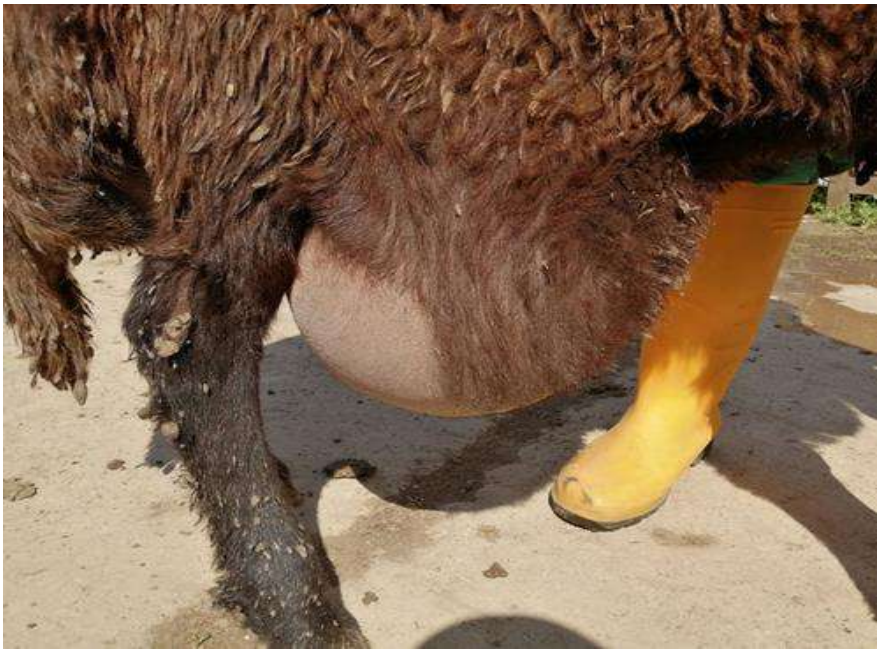

Figure (4-14): photographic picture show over size of hernia sac 30 days post induced hernia.

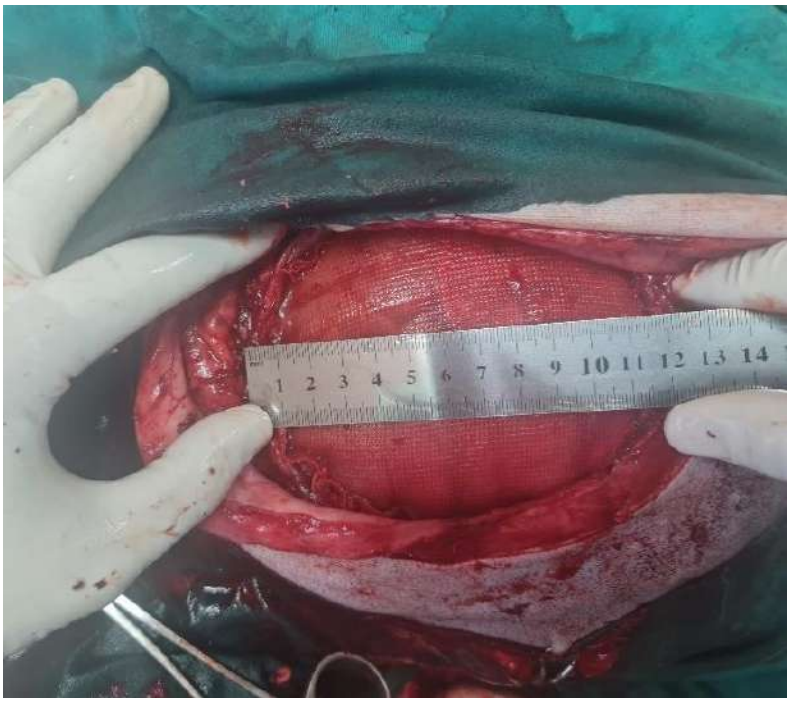

Figure (4-15) Photographic picture show increased the diameter of hernia ring.

Additionally, the daily follow-up for a few common complications.

4-5 Histopathological Examination

The result of the 7th day post-hernioplasty in G1, G2 and G3 showed that presence of space represented the remaining of surgical mesh in site of insertion, these vacuoles surrounded by hyperplasia of fibroblasts in response to inflammatory process and to synthesis the arachidonic acid as extracellular matrix, in addition to initial deposition of collagen fibers as crude bundles surrounding these vacuoles which flooded by granulation tissues that contains activated fibroblast, with infiltration of mononuclear inflammatory cells especially macrophages and lymphocytes, all these features of tissue reaction was seen and recorded in all groups, except of that the angiogenesis which define as a newly blood vessels formation was recorded only in G3 (Figures 4-16 and 4-17).

The result of the 15th days post-surgery in control, PRF and Aloe vera groups showed that continuous presence of vacuolar spaces that represented the remaining of surgical mesh, the area around these vacuoles occupied by infiltration of macrophages and lymphocytes which was recorded in few numbers in both PRF and Aloe vera groups, while these cells founded in sufficient numbers in control group. In addition, the newly blood vessels were observed in high numbers in PRF group filling the granulation tissue to facilitate the healing and less in number in Aloe vera group, and recorded in few numbers in control group. The collagen fibers were observed deposited in all groups and associated with edema associated with granulation tissue as a general definition, which observed contained activated fibrocytes and fibroblast (Figures 4-16 and 4-17).

The result of the 30th days post-surgery in control, PRF and Aloe vera groups showed that continuous presence of vacuolar spaces that represented the remaining of surgical mesh, the area around these vacuoles occupied by infiltration of mononuclear inflammatory cells which was recorded in few numbers in PRF in focal distribution in compare to Aloe vera and control groups, these cells mainly were macrophages and lymphocytes. The newly blood vessels were recorded in all groups, but the number of these angiogenic structure still in high numbers in PRF groups and few number in Aloe vera group and less in control group. Deposition of collagen fibers also recorded in all groups expect that the maturation of these fibers was recorded in both PRF and Aloe vera groups, while in control group these fibers are still under deposition and knitting process. This granulation tissue also recorded in all groups, in addition to that these extracellular structures were seen less extended in PRF group than that recorded in Aloe vera and control groups (Figures 4-16 and 4-17).

The result of the 45th days post-surgery in control, PRF and Aloe vera groups showed that presence an area as a vacuolar space that represented the remaining of surgical mesh. In PRF group the site of tissue reaction showed complete healing process with mature collagen fibers which appeared as stretched waved fibers with few depositions of hemosiderin pigmentation which define as a mature granulation tissue. In contrast, the Aloe Vera group showed advance uncompleted stages of wound healing which represented by presence of newly blood vessels, deposition on mature un-waved collagen fibers and few infiltrations of mononuclear inflammatory cells. On other hand, the control group showed progressed stages of healing process, featured by presence of granulation tissue with infiltration of mononuclear inflammatory cells around mesh vacuoles, and immature collagen fibers, with newly blood vessels (Figures 4-16 and 4-17).

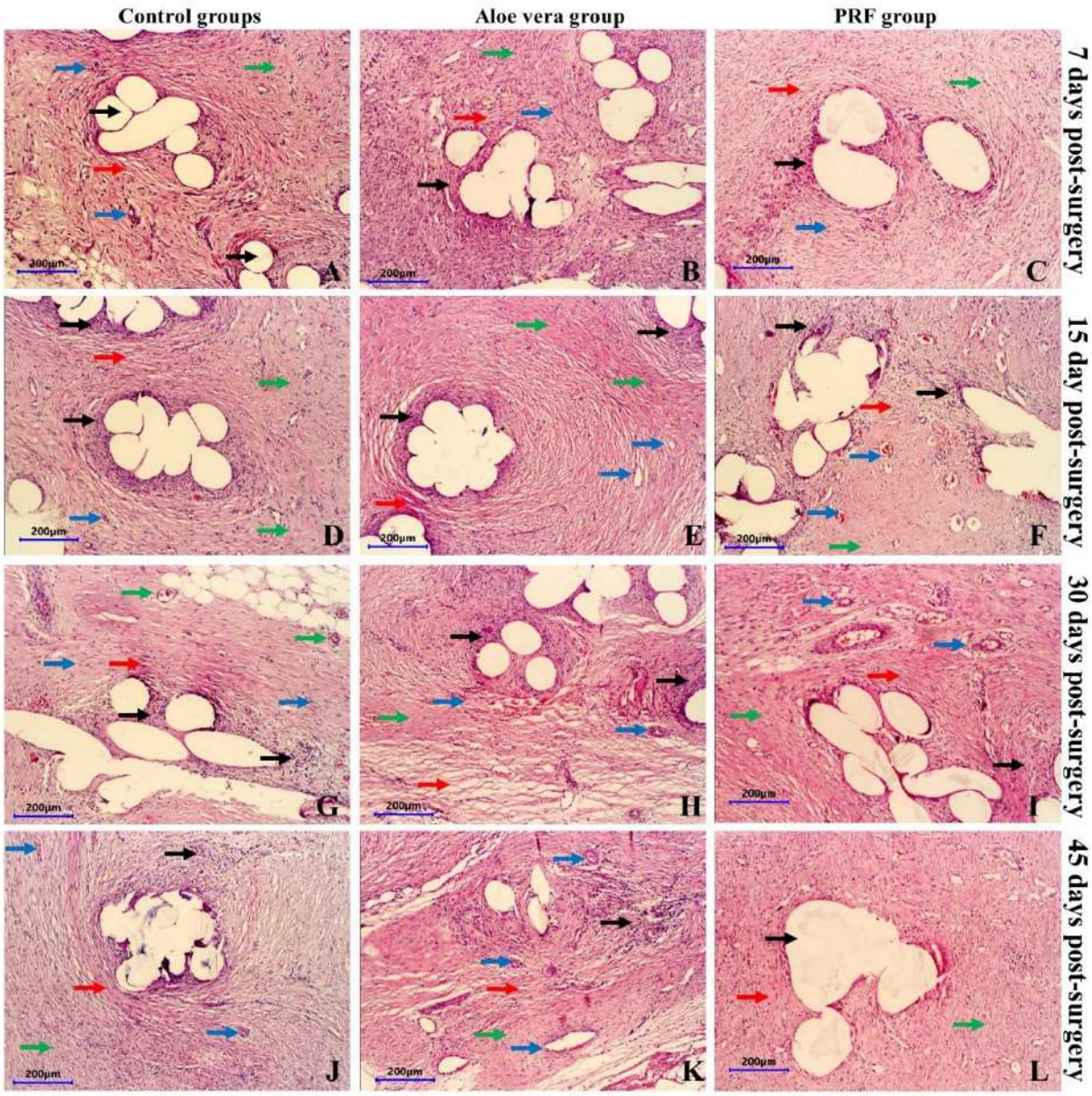

Figure 4-16:photographic image Showed space of surgical mesh (**arrow**), hyperplasia of fibrocytes (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation (**arrow**). Figure B: Showed space of surgical mesh (**arrow**), hyperplasia of fibrocytes (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation (**arrow**). Figure C: Showed space of surgical mesh (**arrow**), hyperplasia of fibrocytes (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation with newly blood vessels (**arrow**). Figure E: Showed few focal infiltrations of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of collagen fibers with edema (**arrow**), granulation tissue formation (**arrow**). Figure D: Showed focal infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), hyperplasia of

fibrocytes (**arrow**), deposition of collagen fibers with edema (**arrow**), granulation tissue formation (**arrow**). Figure F: Showed few focal infiltrations of mononuclear inflammatory cells around surgical mesh (**arrow**), high number of newly blood vessels (**arrow**), deposition of collagen fibers with edema (**arrow**), granulation tissue formation (**arrow**). Figure G: Showed focal infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), hyperplasia of fibrocytes (**arrow**), deposition of collagen fibers with edema (**arrow**), granulation tissue formation with newly blood vessels (**arrow**). Figure H: Showed focal infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels with hemorrhages (**arrow**), deposition of mature collagen fibers with edema (**arrow**), granulation tissue formation with newly blood vessels (**arrow**). Figure I: Showed few infiltrations of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of mature collagen fibers with edema (**arrow**), mature granulation tissue (**arrow**). Figure J: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of immature collagen fibers (**arrow**), maturation of granulation tissue (**arrow**). Figure K: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of mature collagen fibers (**arrow**), maturation of granulation tissue (**arrow**). Figure L: Showed space left by surgical mesh (**arrow**), mature collagen fibers (**arrow**), mature granulation tissue (**arrow**). H&E.

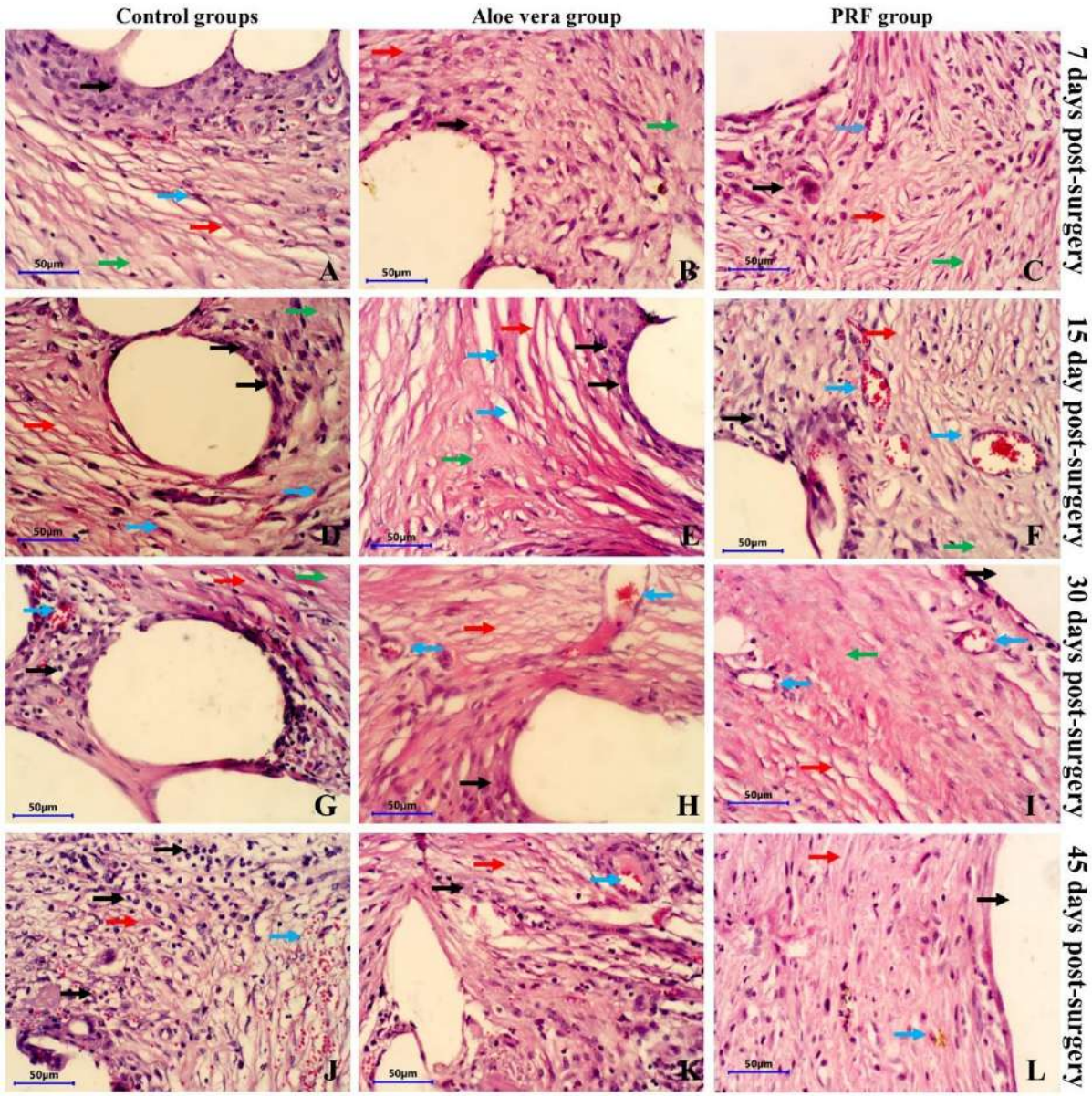

Figure 4-17: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), hyperplasia of fibrocytes (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation (**arrow**). Figure B: Showed few infiltrations of mononuclear inflammatory cells around surgical mesh (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation (**arrow**). Figure C: Showed few infiltrations of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation (**arrow**). Figure D: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), hyperplasia of fibrocytes (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation (**arrow**). Figure E: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), hyperplasia of fibrocytes (**arrow**), deposition of collagen

fibers with edema (**arrow**), granulation tissue formation (**arrow**). Figure F: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of collagen fibers with edema (**arrow**), granulation tissue formation (**arrow**). Figure G: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of collagen fibers (**arrow**), granulation tissue formation (**arrow**). Figure H: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of mature collagen fibers with edema (**arrow**). Figure I: Showed space left by surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of mature collagen fibers with edema (**arrow**), granulation tissue (**arrow**). Figure J: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of immature collagen fibers (**arrow**). Figure K: Showed infiltration of mononuclear inflammatory cells around surgical mesh (**arrow**), newly blood vessels (**arrow**), deposition of mature collagen fibers (**arrow**). Figure L: Showed space left by surgical mesh (**arrow**), mature collagen fibers (**arrow**), hemosiderin pigment deposition (**arrow**). H&E.

4-6 Interleukin 6 (IL-6).

The result of the 7th days post-surgery showed a strong positive expression of IL-6 was recorded in G1, G2 and G3. This high expression was continued to recorded in high expression in the next 15th days post-surgery in all groups. In addition to that expression of IL-6 was also recorded in positive reaction in all groups without any differences in expression. In the 45th days post-surgery the expression in aloe vera and PRF groups were showed decline in expression in weak positive grade of expression in compare to control group were its recorded in positive reaction to IL-6 (Figure 4-18).

4-7 Vascular endothelial growth factor (VEGF).

The result of the 7th days post-surgery showed a strong positive expression of VEGF was recorded only in PRF in a very strong reaction, while this expression was recorded in negative status in both control and Aloe Vera groups. In the 15th days post-surgery, the expression of VEGF was seen in strong positive reaction in PRF group, and in positive reaction in Aloe Vera group, and in weak positive reaction in control group. In 30th days post-surgery the expression of VEGF where positive in both PRF, Aloe Vera and control groups. While in 45th days post-surgery the PRF group was showed a negative reaction to VEGF expression, on other hand, VEGF expression was recorded in a positive reaction in both Aloe vera and control groups (Figure 4-19).

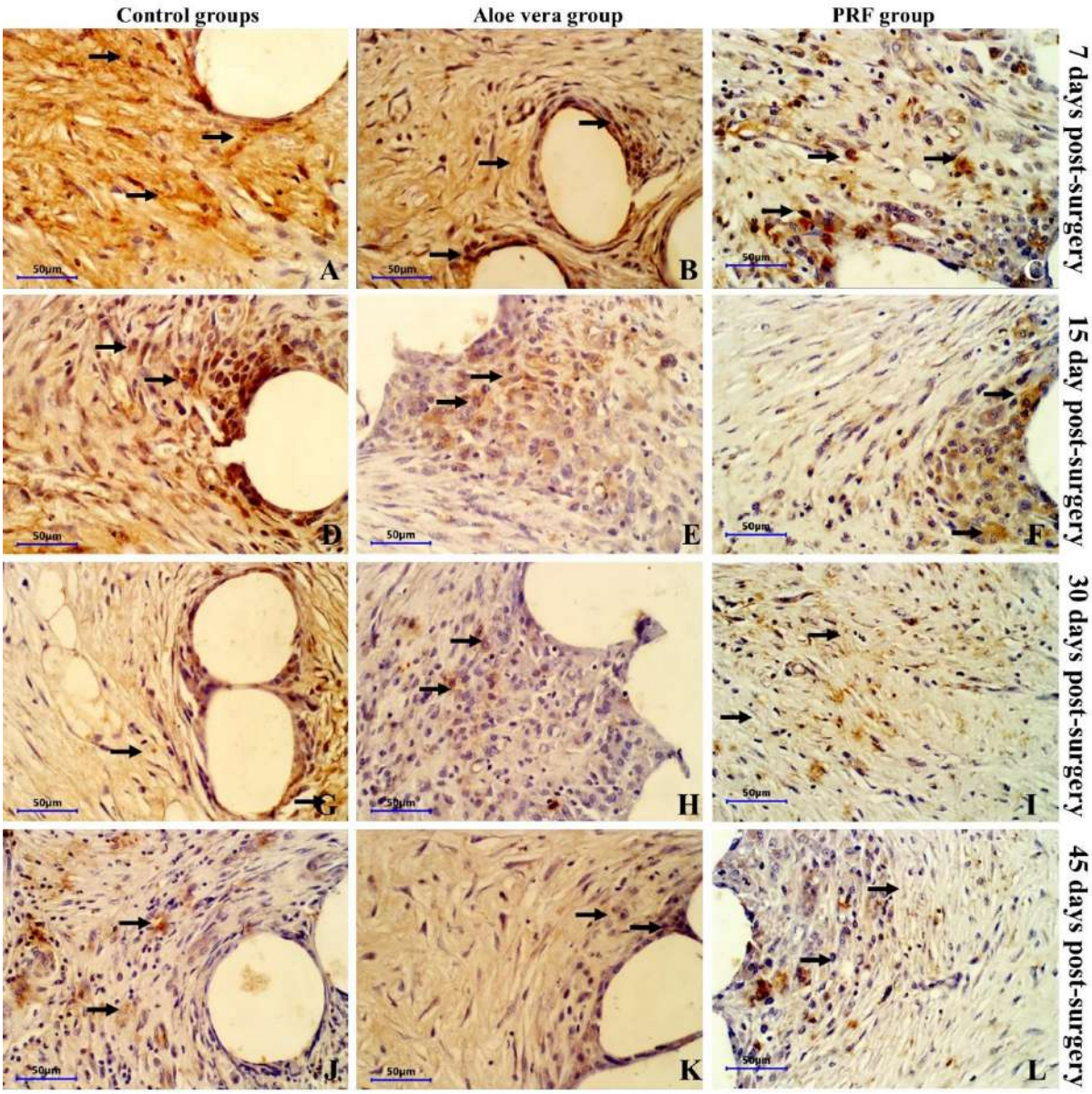

Figure 4-18: Showed strong positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure B: Showed strong positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure C: Showed strong positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure D: Showed strong positive reaction with IL-6 appear as golden-brown patches in cytoplasm of cells around surgical mesh (**arrow**). Figure E: Showed strong positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure F: Showed strong positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure G: Showed positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure

H: Showed positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure I: Showed positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure J: Showed positive reaction with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure K: Showed weak positive reaction in few cells with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure L: Showed weak positive reaction in few cells with IL-6 appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). IL-6 antibody IHC.

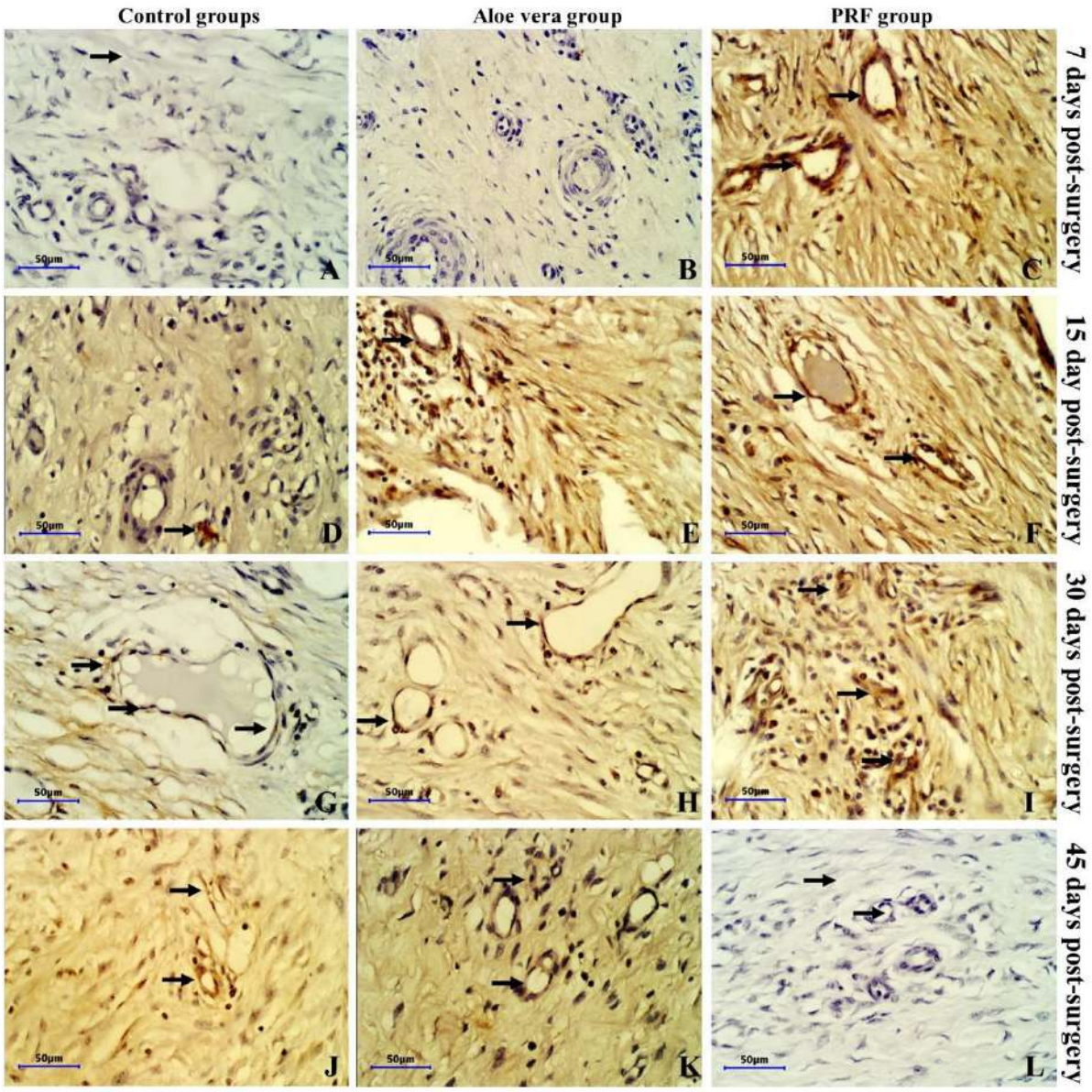

Figure 4-19: Showed negative reaction with VEGF. Figure B: Showed negative reaction with VEGF. Figure C: Showed strong positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure E: Showed positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure D: Showed weak positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure F: Showed strong positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure G: Showed positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure H: Showed positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure I: Showed positive reaction with VEGF appear as

golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure J: Showed positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure K: Showed positive reaction with VEGF appear as golden-brown granules in cytoplasm of cells around surgical mesh (**arrow**). Figure L: Showed negative reaction with VEGF. VEGF antibody IHC.

4-8 Histopathological scoring

4-8-1 inflammatory reaction

The results in the 7th and 15th day post operation showed that the most prominent inflammatory response was recorded in PRF group then in Aloe Vera group in compare with control group, while in 30th, and 45th days post operation the highest inflammatory reaction was recorded in control group, then in Aleo Vera group and in the lowest respond in the PRF group. These results indicate that the PRF group causing trigger of massive inflammatory response to the cut area in order to promote the inflammatory response, then in 45th days post operation these inflammatory responses were dimensioned in compare to Aloe Vera and control group which is also appear significantly at $P<0.05$ (Table 4-1).

Table 4-1: Shows the mean ± stander error values of inflammatory reaction in control and treatment groups at different period post-operation

Group	7 days	15 days	30 days	45 days
Control	0.87±0.01 C	2.08±0.02 C	3.18±0.01 A	1.72±0.02 A
Aloe vera	1.00±0.02 B	2.57±0.04 B	2.94±0.13 B	0.97±0.04 B
PRF	1.33±0.01 A	3.50±0.01 A	2.01±0.11 C	0.57±0.03 C

- Different vertical letters mean presence of significant differences in the same day within different groups at $P<0.05$.

4-8-2 Granulation Tissue Formation

The result in the 7th day post operation showed that a high amount of granulation tissue formation was seen in PRF group then in Aloe Vera group in compare with control group at final stage, while in 30th, and 45th days post operation this image was reflected in which the highest granulation tissue formation was recorded in control group, then in Aleo Vera group and in the lowest formation in the PRF group. These results indicate that the PRF group causing highest initial formation of granulation tissue to form the extracellular matrix to serve migration of inflammatory cells and activated fibroblasts to start their action as fast as possible, then in 45th days post operation the granulation tissue were dissolved and reorganized in order to permit the natural tissue context to be restored which was recorded in PRF group then in Aloe Vera and control group which is also appear significantly at $P<0.05$ (Table 4-2).

Table 4-2: Shows the mean ± stander error values of Granulation tissue formation in control and treatment groups at different period post-operation

Group	7 days	15 days	30 days	45 days
Control	0.89±0.01 C	1.25±0.01 C	2.34±0.02 A	1.97±0.01 A
Aloe vera	1.58±0.01 B	1.98±0.03 B	2.01±0.02 B	1.02±0.01 D
PRF	1.98±0.02 A	2.07±0.02 A	1.57±0.01 C	0.52±0.03 C

- Different vertical letters mean presence of significant differences in the same day within different groups at $P<0.05$.

4-8-3 Angiogenesis

The result in the 7th, 15th, and 30th day post operation showed that a noticeable initial increase in newly blood vessels in PRF group then in compare to Aloe vera and control group during all post operation days. While in 45th days post operation

the result showed decreased in the newly blood vessels formation. These results showed that the content of PRF materials will cause activation the formation of newly blood vessels which considered as essential keystone in promoting the healing process to facilitate bring inflammatory cells and fluid in the site of healing. Later this criterion was decreased to be at the lowest level in the last day of experimental in order to ending the healing process (Table 4-3).

Table 4-3: Shows the mean ± stander error values of newly blood vessels formation in control and treatment groups at different period post-operation

Group	7 days	15 days	30 days	45 days
Control	1.55±0.01 C	1.90±0.01 C	2.21±0.01 C	2.01±0.01 A
Aloe vera	1.67±0.02 B	2.45±0.01 B	2.98±0.02 B	1.51±0.11 B
PRF	2.01±0.01 A	2.89±0.01 A	3.27±0.02 A	1.07±0.01 C

- Different vertical letters mean presence of significant differences in the same day within different groups at $P<0.05$.

4-8-4 Fibrous tissue formation

The results in the 7^{th}, 15^{th}, and 30^{th}, day post operation showed that a noticeable increase in fibrous tissue formation in PRF group in compare to Aloe vera and control group. These results showed that the content of PRF materials can cause increase in amount of fibrous tissue deposition and maturation in order to form the extracellular matrix to help cells to migrate and start their action also help in closure the wound edges. In addition, during the 45^{th} days post operation the amount of fibrous tissue decreased dramatically in PRF group in compare to other groups, this action occurs as soon as these collagen fibers stretched and mature (Table 4-4).

Table 4-4: Shows the mean ± stander error values of Fibrous tissue maturation and deposition in control and treatment groups at different period post-operation

Group	7 days	15 days	30 days	45 days
Control	0.13±0.01 C	0.97±0.02 C	1.10±0.02 C	0.87±0.01 A
Aloe vera	0.32±0.01 B	1.21±0.01 B	1.34±0.11 B	0.77±0.01 B
PRF	0.44±0.01 A	1.40±0.02 A	1.54±0.05 A	0.51±0.01 C

- Different vertical letters mean presence of significant differences in the same day within different groups at $P<0.05$.

4-9 IL-6 expression

The result in the 7th, and 15th day post operation showed that a noticeable increase in the expression of IL-6 as proinflammatory agent in PRF group in compare to Aloe vera and control group. While during the 30th and 45th days post operation these expressions were decreased in compare to Aloe vera and control groups at $P<0.05$. The IL-6 act as proinflammatory agent that helps in vasodilatation and bring more fluids and cells to the healing site which is play a key role in first days of healing. Later its decline in expression will cause starting a new phase of healing and increasing in expression of other cytokines genes that help in complete healing of the wound site (Table 4-5).

Table 4-5: Shows the mean ± stander error values of IL-6 expression in control and treatment groups at different period post-operation.

Group	7 days	15 days	30 days	45 days
Control	1.20±0.01 C	1.75±0.01 C	1.92±0.02 A	1.77±0.01 A
Aloe vera	2.82±0.01 B	2.10±0.02 B	1.73±0.02 B	1.02±0.01 B
PRF	3.01±0.01A	2.57±0.01 A	1.01±0.01 C	0.32±0.05 C

- Different vertical letters mean presence of significant differences in the same day within different groups at $P<0.05$.

4-10 VEGF-expression

The result in the 7^{th}, 15^{th}, and 30^{th} day post operation showed that a noticeable increase in the expression of VEGF-A in PRF group in compare to Aloe Vera and control group. While during the 45^{th} days post operation these expressions were decreased in compare to Aloe Vera and control groups at $P<0.05$. The expression of VEGF-A considered the main feature help in newly blood vessels formation, mainly expressed in the epithelia cells lining capillaries (Table 4-6).

Table 4-6: Shows the mean ± stander error values of VEGF expression in control and treatment groups at different period post-operation.

Group	7 days	15 days	30 days	45 days
Control	1.71±0.01 C	2.07±0.02 C	2.54±0.01 C	1.98±0.01 A
Aloe vera	1.95±0.02 B	2.71±0.02 B	3.11±0.02 B	1.74±0.01 B
PRF	2.59±0.01 A	3.01±0.01 A	3.44±0.03 A	0.89±0.05 C

- Different vertical letters mean presence of significant differences in the same day within different groups at $P<0.05$.

Chapter Five

Discussion

5-1: Post-operative Observations

In this study, Clinical observations indicated Lethargy, slight depression, decreased physical activity, bioactive behavior, and decreased hunger status are minor, non-specific secondary health problems. Poop regularly for the first 48 hours after surgery. The region started to exhibit the typical signs of inflammation, such as redness, heat, swelling, and discomfort, 3 to 5 hours after the procedure. These signs remained and reached their height 24 to 48 hours later. The surgical wounds healed successfully, and during the follow-up periods until the hernias were addressed, no symptoms of bleeding or hematoma, infection or stitches abscess were noticed. This observation concurred with (Riaz *et al.*, 2022; Chen *et al*., 2023). Both the hernial sac's and the hernial ring's sizes varied, as well as their shapes. According to the researcher (Kitessa, *et al*., 2021), the difference in the size of the hernia may be caused by not suturing the edges of the abdominal muscles. Alternatively, it may be caused by individual variations in the size of the abdomen and the motor abilities of the experimental animals. Also, another workers prove that the variations in the measuring size of hernia due to lifting the edges of induced hernia without suturing which allows expansion of the induced wound in different size (Eesa *et al*., 2007; Thanoon, 2012).

5-1-1 Post-operative pain

The intensity of the pain differed between the three groups, where it was most severe in the Aloe Vera group, then the control group, and the least severe was

in the G3, and this was evident through clinical signs of lack of movement grindings of teeth, decrease appetite, breathe too shallow. PRF-mesh repair is a safe and effective option in the treatment of hernias as it couples the safety of physiologically enhanced healing with the efficacy of prompt fixation of the mesh with less pain, so all operative animals in this group returned to normal activities and movement within few days post-surgery this outcome agreed with (Di Nicola and Tebala . 2021).

5-1-2 Seroma

Following hernia surgery, a seroma developed in the lower region of the surgical site, which was clearly visible as a gradual swelling that resembled a sac between two and five days later according to (Ferrer Martínez *et al*., 2023). Seroma was the most common postoperative consequence (26.4%) this result agree with control group in this research with 25%. 16% in Aloe Vera group and 8% in PRF group.

Seroma as a most common post-operative issue of hernia occurs in different ratio according to previous study about (26.4%) of all studied cases this outcome match with current study, the occurrence of seroma after hernioplasty may indicated to failing in hemostasis and bleeding arrest during reconstruction of hernia and excessive manipulation and dissection to subcutaneous tissues which produce excessive dead space and therefore serum and clot blood collected subcutaneously (Al-Sobayil, and Ahmed, 2007 ; Hummadi , and AL-sadi 2011; Liang *et al.*, 2023) , L-PRF clot, PRF membranes, and hyper-acute serum are now being used to fix the mesh during inguinal hernia open mesh repair procedures. Results so far are quite encouraging. PRF has scaffolding qualities and reduces the danger of blood pathogen transmission. In addition, PRF has advantageous anti-inflammatory

qualities as contrasted to cyanoacrylates, which are known for promoting inflammatory tissue reactions. Most importantly, PRF demonstrates robust tissue regeneration capabilities as well as a good fixing capacity. Rapid fibroblast colonization and effective collagen formation in PRF speed up the integration of the mesh while reducing the local inflammatory acute reaction. These components work together to speed up and improve the healing of wounds (Di Nicola, 2020).

5-1-3 Recurrence

The recurrence rate of hernia varies depending on many factors such as the size of the hernia, the repair technique, the type of hernia and many other factors, which usually ranges between 2-6 % (Katzen, *et al.*, 2022) .In this study the results exhibited no recurrence rate in as contrast another studies which used another technique of suturing onlay technique which associated with occurrence of incisional hernia (Al-Sobayil, and Ahmed. 2007; Eesa, *et al.*, 2007; Liang *et al*., 2023).

The using sublay technique might be prevent the incidence of hernia recurrence as well as this technique provided non-tension fixation and the load also distributed equally over the mesh and reduce bulging, this study is relatively short follow-up period and the size of the experiment. On other side, this study disagree with another worker who suggest that the incidence of hernia occurrence with high rate of recurrence after reconstructed with synthetic mesh as compare to biological mesh (Rathore *et al*., 2018). The short time of this study may be the reason especially most recurrences occurs several months even years post hernioplasty (Chen, *et al*., 2023).

5-1-4 Inflammation and abscess formation

The area of operation appeared without serious complications no signs of hematoma or stitches a abscessation along the period of treatment except in control group there were formation local abscess and inflammatory signs throughout the periods of follow-up in three of three animals, the abscess observed at the fold created by the polypropylene mesh, which located directly above the implanted mesh, whereas there were no abscess formation observed in another groups of current study. In first treatment group there was no inflammatory signs or any infection or focal abscess formation exhibited at the site of implant and operation this suggested due to the antibacterial effect of Aloe Vera in animals of the first treatment group, Aloe Vera which help in infection tolerance and decrease the possibility of bacterial contamination at the surgical site and improve wound healing this coincided with (Hekmatpou, *et al*., 2019), who reported about using Aloe Vera as antibacterial, anti-viral, anti-inflammatory . Because of the ethanol extract containing of Aloe Vera leaves and roots is applied on these bacterial and fungal strains in different concentrations (Danish, *et al*., 2020). Applications of sterilized Aloe Vera extract, intraperitoneal dexamethasone and piroxicam indicated successful outcome in preventing adhesions of peritonea (Shahzamani, *et al*., 2012). Also Aloe Vera have been a potential effect on prevention Salmonella infection. Different works was done on Aloe Vera for investigation different properties as Antiulcer activity, Anti hypercholestermic, Antifungal and Antibacterial activity, Antiacne, Cardiac stimulant, Moisturizer, Protection of skin and Immunomodulator (Bhuvana, *et al*., 2014).

In second treatment group with PRF same outcome obtained, it has antimicrobial activity according (Feng.*et al*., 2020) who studied the antibacterial effect of PRF But this study dis agree with (Sartelli, *et al*., 2023), which prove no any effect of PRF on healing process this may be due to the anatomical variations between humans and sheep and the nature of lying on the abdomen as well as the inability to maintain surgical drainage in sheep. Since the PRF contains a huge amount of cytokines, PRF exert as chemokine reservoir, which secret inflammatory cytokines to promote the healing process and give addition feed effect to the naturally cytokines produce due to wound formation, these massive pulses of cytokines cause rapid expression of IL-6 gene in the site of action to increase IL-6 formation for affect cells and PRF materials, to exert it effect by increase in chemical attraction of phagocytes to neutralize the causative agent, removal of dead tissues, and promote the healing process specially newly blood vessels formation (Nasirzade, *et al.,* 2020).

5-2 Ultra-Sonographic Assessment

Ultrasound tool is a beneficial effective device for investigation, monitoring the post-surgical complications of hernia explore any issue suturing technique. (Hummadi, and AL-Asadi, 2011)It is a noninvasive technique used for monitoring postoperative tissue healing (Vilar, *et al*., 2011). as investigation technique for repaired Achilles tendon rupture (Allawi *et al*.,2019) and experimental cystotomy of urinary bladder in dogs (Alhamdany, and Alkattan, 2019)and for investigation the Induced Large Ventro-lateral Hernia in Bucks(Hummadi, and AL-Asadi, 2011). It plays an crucial role in the assessment and monitoring along operation and post-surgical treatment, so this technique permits exanimating and identifying the status of mesh, diagnosis of complications such as postoperative seroma and wound dehiscence and failing of sewing technique (Crespi, *et al*.,2004). In the

first treated group with Aloe Vera leaf gel, the granulation tissue begins from the second week and fibrosis appear at 30 days which indicate the usefulness of Aloe Vera in accelerating healing process due to the complete healing at 45 day the subcutaneous tissue appears normal echotexture with a clear mesh. From results of ultrasound at zero time the Mesh appear as thin echogenic white colored line inside the homogenous midechogenicity muscle mass, thereafter, re-examination with ultrasound of control group there were a hypoechogenic space indicate inflammatory process with exudate accumulation around the mesh, furthermore in treated group the hypoechoic areas appear early during the experiment then disappear and replaced by echogenic areas represents granulation tissue from the second week. The use of the ultrasound device to follow up the healing of hernias gave a clear picture of the difference between the three groups in terms of the occurrence of seroma and the nature of the complications associated with the healing process which agreed with (Kumar, *et al*., 2022).

The present study verified that abdominal wall healing can be monitored perfectly by ultrasonography. Curvilinear arrays with low frequency transducers also offer improved resolution and dependability for scanning of abdominal wall defects and the use of 5.5 MHz transducers are effective for assessing and contrasting the progressive healing processes in the abdominal wall hernias between the three study groups.

5-3 Laparoscopic Assessment

Laparoscopy now is the standered devise for examination and treatment method which permits visualization, and reduce risk of bleeding less time consuming (Awaiz, *et al*., 2015). In this study laparoscopic examination at 45 days post-surgery show degree of adhesion between omentum, repaired site and internal organ with

less degree in G2 and G3compare with G1 this considers advantageous for sealing incision this played a role in preventing leakage and serous contamination in the treated group there were no complications and less adhesion this might be due to the role of Aloe Vera as a bioactive material. (Hashemi *et al*., 2015)

Laparoscopic surgery's assessment of adhesion intensity revealed complete adhesion of the omentum with a polypropylene mesh, as well as adhesion of the suture area. The stability of adhesion increased with the periods, as it was observed that the congestion gradually decreased, and there was no intestinal or other internal organ adhesions. This technique gave a clear visualization and shape of the progress and state of adhesion between the surgical mesh and the Omentum (Alkattan, *et al*., 2014- Awaiz, *et al*., 2015).

5-4- Histopathological and immunohistochemistry assessments

The angiogenic activity of PRF has a great effect on wound healing; this effect is appeared as increasing expression of VEFG in the epithelial cells of blood vessels in the wound site in the epithelial cells of new blood vessels, the increase in the number of these vessels will bring more fluid to dilute the causative agent effect and bring more cell to the site of reaction to faster the healing process and these cells also act to remove any cellular debris that accumulates in the wound site (Veith, *et al*.,2019; Everts, *et al*., 2023). Many studies recorded a great effect of Aloe Vera gel as good wound healing media, but the exact mechanism that induce and accelerate the wound healing is still unclear (Davis, *et al*., 1987; Chelu, *et al*., 2023). The Aloe Vera showed that it is a good angiogenic material, in which it is shown that the Aloe Vera gel have three angiogenic materials ß-sitosterol, ß -sitosterol glucoside, and aloe emodin (Risau, 1997).in which ß-sitosterol showed to have a similar chemical structure to cholesterol, which is used widely in pharmacological industry as a drug

to reduce the level of cholesterol and enhance the level of LDL in blood and reduce the size of human colon cancer HT-29 (Awad, *et al*., 1998), in addition, ß-sitosterol have a great ability to induce plasminogen activator which have a direct effect of VEGF gene by increase it is expression which lead to increase in endothelial cell proliferation and increase in the number of newly blood vessels (Ismail, *et al*.,2021; Akbarian, *et al*., 2022).

In addition, the PRF can greatly increase the differentiation of epithelial cells and their proliferation; these processes help in fast reepithelization and promote healing (Serafini, *et al*., 2020; Pavlovic, *et al.,* 2021). The aloe Vera gel contains aloe emodin which shown that have anti-inflammatory response alone and with ß-sitosterol cause increase in epithelia cell proliferations which help in the reepithelization process and wound healing (Dong, *et al*., 2020).

Since the PRF contains a huge amount of cytokines, PRF exerts as a chemokines reservoir, which secrets inflammatory cytokines to promote the healing process and give an additional feed effect to the natural cytokines produced due to wound formation; these massive pulses of cytokines cause rapid expression of IL-6 gene in the site of action to increase IL-6 formation for affect cells and PRF materials, to exert its effect by the increase in chemical attraction of phagocytes to neutralize the causative agent, removal of dead tissues, and promote the healing process especially newly blood vessels formation (Veith, *et al*.,2019). On other hand, aloe vera contains many bioactive materials such as anthraquinones, hormones, vitamins, proteins, and sterols with organic compounds (Maan, *et al*., 2018), all these materials shown to have effect on the IL-6 gene and increase their expression in site of healing after general or systemic administration (Kistner, *et al*., 2022).

IL-6 play an important role in the first three days of the healing process, and the decline in IL-6 concentration leads to an increase in IL-12 concentration in the wound site, which promotes the deposition of collagen fibers and their maturation, so the rapid formation of IL-6 (pro-inflammatory cytokines) means it will rapidly decrease in its concentration, that means rapid elevation in the IL-12 concentration (post-inflammatory cytokines) these will lead to rapid granulation tissue formation, collagen deposition, and maturation, all these accelerating events will lead to shorten the time for the wound to be healed (Johnson, *et al*., 2020).

Chapter Six

Conclusions & Recommendations

6-1 Conclusions

1- Using PRF as natural bioactive material in repairing experimental abdominal hernia have beneficial value as reducing the rate of post-operative pain, adhesion and inflammation.

2- Using Aloe Vera gel as natural bioactive material, prevent infection and abscessation and improve healing process.

3- Histopathological and immunohistochemistry investigations emphasize and the impact of using PRF in activation of process of hernia.

4- Impact of both PRF and Aloe Vera gel as natural bioactive material in decreasing the incidence and severity of post-operative seroma in sheep.

5- Using of modified sublay technique for hernioplasty with PP mesh which was easy application, safe, beneficial technique with minimum complications no signs of recurrence after reconstruction of large abdominal wall hernias.

6- Ultrasonograph is useful tool to determine the healing progress and revel complications associated abdominal wall healing.

6-2 Recommendations

1- Suggest using acellularised tunica vaginitis and submucosal layer of intestine in reconstitution ventro- lateral hernia

2- Extending the follow up periods postoperative more than 45 days to follow up the healing process and observation of any post-operative complications such as recurrence, contraction of surgical mesh and migration.

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جامعة الموصل
كلية الطب البيطري

دراسة مقارنة لاستخدام هلام الصبار والليفين الغني بالصفيحات الدموية في اصلاح الفتق البطني المستحدث جراحيا في الاكباش

ابراهيم احمد زيدان حسين

أطروحة دكتوراه
الطب البيطري / الجراحة البيطرية

بإشراف
الأستاذ الدكتور

ليث محمود داؤد القطان

الاستاذ الدكتور(مشرف ثاني)
سيفان سعد فاضل المحمود

2024م 1445هـ

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أطروحة تقدم بها

ابراهيم احمد زيدان حسين

إلى
مجلس كلية الطب البيطري في جامعة الموصل
وهي جزء من متطلبات نيل شهادة الدكتوراه فلسفة
في اختصاص الطب البيطري / الجراحة البيطرية

بإشراف
الأستاذ الدكتور
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سيفان سعد فاضل المحمود

2024م **1445هـ**

الخلاصة

تم تصميم هذه الدراسة لتقييم عملية الشفاء لإصلاح فتق جدار البطن الكبير المستحث تجريبياً باستخدام شبكة البولي بروبيلين (PP)وحدها أو المعززة باستخدام هلام الصبار أو المعززة بالفيبرين الغني بالصفائح الدموية (PRF) تم استخدام ستة وثلاثون كبشاً بالغاً قسمت عشوائياً إلى ثلاث مجموعات، مجموعة ضابطة ومجموعتين معاملتين، بواقع اثني عشر حيواناً لكل مجموعة .وبموجب بروتوكول التسدير العميق والتخدير الموضعي، تم تجهيز موقع العملية بشكل معقم، واحداث فتق جدار البطن بقطر 10 سم، ثم تركه لمدة شهر بعد ذلك، ومن ثم إجراء عملية اصلاح الفتق وفق ما يلي¬ :

المجموعة 1: (السيطرة) تم إصلاح الفتق باستخدام شبكة PP لوحدها وتم تثبيت الشبكة تحت العضلات بطريقة محورة .

المجموعة 2: تم إصلاح الفتق باستخدام شبكة PP مع هلام الصبار المحضر وتم تثبيت الشبكة تحت العضلات بطريقة محورة

المجموعة 3: تم إصلاح الفتق باستخدام شبكة PP مع PRF. وتم تثبيت الشبكة تحت العضلات بطريقة محورة تمت مراقبة عملية الشفاء وترميم جدار البطن في موقع الفتق المستحدث على مدار 45 يومًا من خلال الفحوصات السريرية والموجات فوق الصوتية والجراحة المنظارية والفحوصات المجهرية والكيميائية المناعية .في جميع حيوانات التجارب، أظهرت الفحوصات السريرية للفتق بعد الاصلاح وإعادة بنائه مشاكل صحية ثانوية غير محددة .بينما أظهر الفحص بالموجات فوق الصوتية في الأيام 7 و15 و30 و45 بعد الاصلاح أن علامات الفتق تضاءلت تدريجياً في نهاية الدراسة بينما أشارت الفحوصات التنظيرية إلى التصاق كامل للثرب مع شبكة البولي بروبيلين المزروعة وحواف جدار البطن في منطقة الفتق .زاد ثبات الالتصاق مع مرور الوقت، ولم تكن هناك التصاقات معوية أو أي التصاقات بالأعضاء الداخلية الأخرى، علاوة على ذلك، أشار التقييم النسيجي إلى وجود عملية شفاء مبكرة في الجموعة 3 والتي تمثلت بوجود عدد كبير من الأوعية الدموية الجديدة مع ترسيب ألياف الكولاجين في حين أن اختبارات الكيمياء المناعية لل IL-6 اشارت في كل من المجموعة الضابطة ومجموعة PRF إلى رد فعل إيجابي قوي في الأيام من 7 إلى 15 بعد عملية رأب الفتق والتي ظهرت كحبيبات بنية ذهبية في سيتوبلازم الخلايا حول الشبكة الجراحية، ولكن في المجموعة الثالثة في اليوم 30 بعد الجراحة تمت الإشارة إلى تفاعل إيجابي ضعيف في عدد قليل من الخلايا مع الجسم المضاد .IL-6 IHC إلى جانب التعبير الكيميائي المناعي لـ VEGF في المجموعة الثانية في اليوم السابع

أشار إلى تفاعل سلبي، بينما في اليوم 15 إلى اليوم 45 بعد الجراحة أشار إلى تفاعل إيجابي مع عامل نمو بطانة الأوعية الدموية (VEGF) الذي ظهر على شكل حبيبات بنية ذهبية في سيتوبلازم الخلايا المحيطة بشبكة PP أشارت نتائج تحليل درجات التفاعل الالتهابي إلى اختلاف الاستجابة بين أعلى معدل تفاعل التهابي ظهر في مجموعة السيطرة يليه المجموعة الثانية وأعلى معدل ظهر في المجموعة الثالثة في هذه المجموعة كانت كمية تكوين الأنسجة الحبيبية هي الأدنى كانت الأوعية الدموية وما تلاها من أوعية دموية جديدة موجودة وزادت على طول فترة ما بعد الجراحة خاصة في المجموعة الثالثة، لكن عدد تكوين الأوعية الدموية الجديدة انخفض في اليوم 45 خاصة في هذه المجموعة الثالثة تليها المجموعة الثانية وكان هناك اختلافات معنوية عند $P < 0.05$. زاد ترسب الأنسجة الليفية بشكل ملحوظ من اليوم السابع إلى اليوم الثلاثين بعد العملية خاصة في المجموعة الثالثة مقارنة بالمجموعتين الأخريين .على الجانب الآخر بعد اليوم 45 بعد الجراحة، انخفضت كمية ترسب الأنسجة الليفية بشكل كبير في المجموعة الثالثة مقارنة بالمجموعات الأخرى، .في الختام، فإن استخدام PRF لإصلاح الفتق يقلل من حدوث الألم والالتهاب بعد العملية الجراحية، وتؤكد فحوصات الكيمياء النسيجية والمناعية على تعزيز عملية شفاء الفتق وتسهيل تكوين أوعية دموية جديدة , إلى جانب استخدام هلام الصبار يمنع العدوى وتكوين الخراج وتعزيز الشفاء.