International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

A Comparative Study of Honey Impregnated Dressing on Chronic Wounds Compared to Conventional Dressing

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Abstract

Chronic non-healing wounds pose a major clinical challenge due to persistent inflammation, infection, and impaired tissue regeneration. Honey, with its antibacterial, anti-inflammatory, osmotic, and debriding properties, has re-emerged as an effective natural dressing. This prospective comparative study evaluated the effectiveness of honey-impregnated dressings versus conventional povidone-iodine moist dressings in chronic wounds. Patients were assessed for wound severity, granulation tissue formation, exudate, pain scores, and healing progression. Honey dressings demonstrated faster reduction in wound severity, earlier and more extensive granulation tissue formation, improved autolytic debridement, and superior overall healing outcomes compared with conventional therapy. Honey is an effective, low-cost alternative to standard dressings and significantly accelerates healing in chronic wounds.

INTRODUCTION

Honey is the oldest known wound dressing. Its uses date back to ancient India. Composed of 80% sugar and 17% water, this supersaturated natural substance used for wound dressing. Its high osmolarity, phytochemicals, and enzymatic production of hydrogen peroxide inhibit bacterial growth, while its acidic pH and autolytic debridement, decrease inflammation and improve blood circulation to enhancing epithelialization and healing with minimal scar tissue. The subject of this review is whether studies show that honey's wound healing properties make it a better wound dressing by decreasing the healing time of chronic wounds, compared to conventional dressing [1]

Honey could be used instead of high-tech products such as the new recombinant growth factors. This may receive low priority in modern protocols, but should rate highly in resource-based health delivery. In this respect, honey appears superior to the expensive modern hydrocolloid wound dressings[2].

Honey is known to increase nitric oxide end products and decrease the prostaglandin levels[3]. The acidification of wounds can enhance healing due to honey's low pH. Honey's low pH can enhance off loading oxygen from hemoglobin in capillaries. It can also suppress protease activity in wounds because of non-neutral pH which is not favorable for their activities4.Increased protease activity in wounds can either slow or stop healing by destroying growth factors and the protein fibers and fibronectin in wounds, which is necessary for the activation of fibroblasts and migration of epithelial cells. This protease activity is a result of extra inflammatory reactions4.The anti- inflammatory activity of honey can eliminate this obstacle to healing. The antibacterial activity of honey works by removing infectious

bacteria stimulating the inflammatory response. Honey has debriding action which helps to reduce the sources of bacteria and hence prevent further inflammatory reactions[4].

Role of conventional wound dressing

The role of a wound dressing is to provide the optimum conditions for wound healing, whilst protecting the wound from further trauma and invasion by pathogenic microorganisms. It is also important that the dressings can be removed atraumatically, so as to prevent further damage to the wound surface during dressing changes[5].

For the most serious types of wounds, such as burns and chronic ulcerations, which produce large quantities of exudates, it is generally accepted that moist wound therapy [conventional dressing] by using H2O2 and betadine plays an important role in effective treatment It is necessary to keep the wound bed moist to prevent cell death by desiccation, to provide a favourable environment for fibroblast proliferation and to allow re-epithelialisation by the migration of keratinocytes from the wound edges, across the surface of the newly formed granulation tissue[5]. It is important however, to maintain a balance in moisture levels, as excess wound fluid can contribute to an increase in bacterial colonisation of the wound and can adversely affect the surrounding area by maceration of the healthy tissue[5].

Aim and Objectives

- The aim of this study is to study the effect of Honey on Treatment for Chronic Wounds Compared to Standard Therapy

Primary objectives-

- To assess the pre and post-test level of severity of wound among patients of experimental group.
- To assess the pre and post-test level of severity of wound among patients in control group.
- To compare the pre and post-test level of severity of wound among patients in experimental and control group

Review of Literature

This part of dissertation is discussed under following headings:

1. **Epidemiology of chronic non-healing wounds**
2. **Etiopathogenesis of chronic non-healing wounds**
3. **Management of chronic non-healing wounds**
4. **Healing and factors affecting wound healing process**
5. **Management of chronic non-healing wounds and role of honey**
6. **Studies conducted in the past on similar topic**

1. Epidemiology Prevalence of chronic non-healing wounds

Chronic non-healing wounds are defined as non-healing wounds that have failed to proceed through the orderly process that produces satisfactory anatomical & functional integrity or that have proceeded through the repair process without producing adequate anatomical & functional result.[1] The prevalence of chronic wound is high, with approximately 1-3% of global population affected by chronic non-healing wounds and this prevalence is known to increase with age. In terms of duration, if the wound fails to heal or shows no Sign of recovery within 12 weeks, it is considered a chronic wound. Predisposing factors

may affect the tissue perfusion causing chronic wounds such as vascular non-healing wounds, associated with metabolic disorders such as diabetes causing diabetic foot non-healing wounds. [2]

Chronic non-healing wounds shows no tendency to heal after 3 months of appropriate treatment or is still not fully healed at 12 months.[18] The incidence of ulceration is rising as a result of the ageing population and increased risk factors for atherosclerotic chronic non-healing wounds such as smoking, obesity, and diabetes. Non-healing wounds can be defined as wounds with a "full thickness depth" and a "slow healing tendency". Non- healing wounds of skin can result in complete loss of the epidermis and often portions of the dermis and even subcutaneous fat. [19]

Chronic wounds of the lower legs is a relatively common condition amongst adults, and ulcer symptoms usually in chronic non-healing wounds increasing pain, friable granulation tissue, foul odor, and wound breakdown instead of healing. This results in social distress and considerable healthcare and personal costs. [20,21] Since numerous factors lead to lower non-healing wounds ulceration, it is essential that health professionals adopt an interdisciplinary approach to the systematic assessment of the individual in order to ascertain the pathogenesis, a definitive diagnosis, and optimal treatment required. A correct diagnosis is essential to avoid inappropriate treatment that may delay wound healing, cause deterioration of the wound, or harm the patient.

Chronic non-healing wounds is reported to have impact on virtually every aspect of daily life: pain is common, sleep is often impaired, mobility and work capacity tend to be restricted, and personal finances are often adversely affected. It is also known that social activities are restricted due to fear of injury and negative body image. Chronic non-healing wounds is usually associated with significant morbidity, high cost of healthcare, loss of productivity, and reduced quality of life. [18-29]

Epidemiology

Chronic non-healing wounds affect 0.6–3% of those aged over 60 years, increasing to over 5% of those aged over 80 years. Chronic non-healing wounds is a common cause of morbidity, and its prevalence in the community ranges from 1.9% to 13.1%.[23] It is thought that the incidence of ulceration is rising as a result of aging population and increased risk factors for atherosclerotic chronic non-healing wounds such as smoking, obesity, and diabetes. In the course of a lifetime, almost 10% of the population will develop a chronic wound, with a wound-related mortality rate of 2.5%.[21]

According to the Wound Healing Society, about 15% of older adults in the US suffer from chronic wounds, chronic non-healing wounds predominantly venous stasis non-healing wounds, pressure non-healing wounds (bedsores), and diabetic (neuropathic) foot non- healing wounds. Every year 2 to 3 million more Americans are diagnosed with various types of chronic wounds. [24] Estimate of annual incidence of non-healing wound in the UK and Switzerland are 3.5 and 0.2 per 1000 individuals, respectively. The prevalence of vascular ulcer in the US is estimated at 500,000 to 600,000 and increases with age. [25,26]

According to the study in Ireland the prevalence was 0.12% but it was 1.03% in the patients aged 70 years and over. Women were twice as likely to be affected. Venous disease accounted for 81% of non-healing wounds and arterial disease for 16.3%, while ulceration due to diabetic neuropathy and rheumatoid vasculitis was unusual. Non- healing wounds healing wounds are an important source of morbidity in our ageing population. [27] In Brazil, a study conducted in Botucatu, São Paulo, reported a

35.5% prevalence of varicose veins and 1.5% prevalence of severe chronic venous insufficiency with an ulcer or ulcer scar. [28] The peripheral artery disease, the circulatory disease commonly associated with non-healing wounds, affects about 8 million Americans and 12–20% of Americans of age group 65–72 years. It is estimated that there are over 7.4 million pressure non-healing wounds in the world where estimation was possible, that is, chronic non-healing wounds the vast number of developing countries. [29]
In Western Australia (WA) in 1994, non-healing wounds healing wounds were found to affect 1.1 per 1000 population (0.11%-point prevalence). This study demonstrated that 24% of the non-healing wounds were present for 1 year, 35% had a problem of ulceration for 5 years, 20% had experienced 10 or more episodes of ulceration, and 45% of sufferers were housebound. [30]
According to a study carried out in Germany, venous insufficiency was the dominating causative factor in 47.6% and arterial insufficiency in 14.5%, and 17.6% of non-healing wounds were due to combined arterial and venous insufficiency. Rarer causes chronic non-healing wounds vasculitis (5.1%), exogenous factors (3.8%), and pyoderma gangrenosum (3.0%).[31]
While there are few Indian studies on the epidemiology of chronic wounds, one study estimated the prevalence at 4.5 per 1000 population. The incidence of acute wounds was more than double at 10.5 per 1000 population. [32]
According to data from epidemiological studies, the incidence of chronic non-healing wounds in surgically hospitalised patients in China is 1.5% to 20.3%. In one study, of the 580 wound areas in 489 patients, 366 or 63% were non-healing wounds on the lower extremities. [33,34]
The period prevalence of non-healing wounds healing wounds in New Zealand has been estimated at 79 per 100,000 per year, although capture-recapture analysis suggests a more accurate estimation, which is between 393 and 839 per 100,000 per year.[35] Prevalence of non-healing wounds increases dramatically with age, although non-healing wounds can occur in quite young people and there are records of people suffering with venous non-healing wounds for up to 60 years.

2. Etiopathogenesis of chronic non-healing wounds

Etiology of chronic non-healing wounds

It has been reported that non-healing wounds related to venous insufficiency constitute 70%, arterial disease 10%, and non-healing wounds of mixed etiology 15% of non-healing wounds presentations. [36]
The remaining 5% of non-healing wounds result from less common pathophysiological causes, and this latter group comprise considerable challenges in diagnosis, assessment, and management. [37]
In the Western world, non-healing wounds are mainly caused by venous insufficiency, arterial insufficiency, neuropathy, diabetes, or a combination of these factors (Table 1). [38] Venous non-healing wounds are the most common type of non-healing wounds, accounting for approximately 70% of cases. Arterial disease accounts for another 5% to 10% of non-healing wounds; most of the others are due to either neuropathy (usually diabetic) or a combination of those diseases.[38,39] The study from India shows that etiology of chronic wounds systemic conditions such as diabetes, atherosclerosis, tuberculosis, and leprosy. Other major causes of chronic non-healing wounds venous non-healing wounds, pressure non-healing wounds, vasculitis, and trauma. The study report stated that inappropriate treatment of acute traumatic wounds was the most common cause of the chronic wound. [32]
Chinese study shows that the principle etiology (67%) of ulceration is trauma or traumatic wounds

compounded by infection. Diabetic non-healing wounds, venous non-healing wounds, and pressure non-healing wounds accounted for 4.9%, 6.5%, and 9.2%, respectively. The majority of these wounds were seen in farmers and other agricultural workers. [23,24]

It is useful to divide non-healing wounds into those occurring in the gaiter area and those occurring in the forefoot because the aetiologies in these two sites are different. At least two etiological factors can be identified in one third of all lower limb non-healing wounds. Venous non-healing wounds most commonly occur above the medial or lateral malleoli. Arterial non-healing wounds often affect the toes or shin or occur over pressure points. Neuropathic non-healing wounds tend to occur on the sole of the foot or over pressure points. [40,41]

Table 1: Causes of non-healing wounds[36]

Vascular	Venus
	Arterial
	Mixed
Neuropathic	Diabetes
	Tabes
	Syringomyelia
Metabolic	Diabetes
	Gout
	Prolidase deficiency
Haematological	Sickle cell disease
	Cryoglobulinemia
Trauma	Pressure
	Injury
	Burns
Tumors	Basal cell carcinoma
	Squamous cell carcinoma
Infection	Bacterial
	Fungal
	Protozoal
Panniculitis	Necrobiosis lipoidica
	Fat necrosis
Pyoderma	Gangrenosum
Special	Hypertensive ulcer

Patients with reduced mobility or obesity may develop ulceration in the gaiter area because of venous hypertension resulting from inadequate functioning of the calf muscle pump. The commonest causes of vasculitis non-healing wounds are rheumatoid arthritis, systemic lupus, and polyarteritis nodosa. The blood dyscrasias that most commonly lead to non-healing wounds are sickle-cell disease, thalassaemia, thrombocythemia, and polycythaemia rubra vera.[39] Other haematological disorders associated with the development of non-healing wounds are leukaemia, hereditary spherocytosis, thrombotic thrombocytopenic purpura, granulocytopenia, and polyclonal dysproteinaemia.[22] Non-healing wounds related to haematological disorders generally result from microcirculatory chronic non-

healing wounds. [41]

Microcirculatory and vascular disorders that can result in atypical non-healing wounds Raynaud's phenomenon, Martorell's non-healing wounds, and cutaneous vasculitis. There are numerous disorders that can result in neuropathy of the lower legs and associated ulceration due to insensate injury, burns, or pressure non-healing wounds, for example, leprosy, alcoholic neuropathy, and tabes dorsalis. [23]

According to a recent report, chronic kidney disease (CKD), hypertension, and myocardial ischemia may also be associated with increased risk of developing foot wounds that necessitate amputation. Additionally, there are reports of higher rates of malnutrition and deficiencies of vitamins and minerals such as zinc in patients with chronic venous non- healing wounds compared to the general population. [22]

Pathogenesis of of chronic non-healing wounds

Venous Non-healing wounds

The association between ulceration at the ankle and venous disorders of the lower limbs has been known for more than 2000 years. Venous circulation of the lower extremities progresses from the superficial to perforating to deep veins, with valves in each system to ensure unidirectional blood flow. As the calf muscles contract, the pumping action causes the blood to flow from the deep veins into the inferior vena cava. Disease of these pathways results in venous insufficiency. Venous insufficiency is the most common cause of lower-non-healing wounds, accounting for nearly 80% of all cases. Of the approximately 7 million people in the United States with venous insufficiency, approximately 1 million develop venous non-healing wounds.[41] Approximately 1% of the population will suffer from non-healing wounds at some point in their lives. Chronic venous non-healing wounds has an estimated prevalence of between 0.1% and 0.3% in the United Kingdom. Prevalence increases with age. The overall prevalence of venous non-healing wounds in the United States is approximately one percent. Venous non- healing wounds are more common in women and older persons. The primary risk factors are older age, obesity, previous non-healing wounds, deep venous thrombosis, and phlebitis. Venous non-healing wounds are often recurrent, and open non-healing wounds can persist from weeks to many years. Severe complications in chronic non-healing wounds cellulitis, osteomyelitis, and malignant change.[42] Patients who develop chronic venous ulcer before their 50th birthday appear to represent a distinct group in terms of aetiology, natural history, and prognosis.

In venous disease, non-healing wounds are usually located in the gaiter area between the ankle and the calf, often on the medial aspect of the leg. Venous non-healing wounds arise from venous valve incompetence. Valvular incompetence in the deep veins causes the vessels to become distended and stretch to accommodate the additional blood flow. The valves are not able to effectively close, which results in retrograde blood flow and venous hypertension.[43] The venous hypertension, leads to leakage of fluid out of the stretched veins into the tissues, causing deposition of a brownish/red pigment in the gaiter area of the leg. Venous ulceration occurs in the gaiter area in 95% of cases especially around the malleolar (the rounded protuberances on the ankle) region. [44] Veins can be damaged by surgery, trauma, or DVT, which causes a back-flow of blood in the venous system at the point of damage. Other causative factors in chronic non-healing wounds include multiple pregnancies, obesity, congenital vein abnormalities, and varicose veins.

Another factor that influences the development of venous non-healing wounds is calf muscle pump failure. Calf pump failure arises from paralysis, immobility, sleeping in a chair with legs dependant for

long periods of time, and fixed ankle joints. The calf muscle, through contraction and relaxation, aids in the flow of blood back to the heart through the veins. Failure of this mechanism causes stasis of blood and increased venous pressure.[45]

There are three major theories of how ulceration develops. (1) Fibrin cuff theory: fibrinogen leaks from dilated capillaries of the epidermis forming a pericapillary fibrin cuff. This is then responsible for a reduced diffusion of oxygenated blood to the tissues resulting in ulceration. (2) Leukocyte entrapment theory: venous hypertension reduces the pressure gradient between the arteriolar and venular end of the capillaries. This results in sluggish movement of the blood within these capillaries and increases the adherence of blood cells to the endothelium. Inflammatory mediators (ICAM-1, VCAM-1) and reactive oxygen species are then released resulting in the obliteration of functioning capillary loops aggravating ischemia and result in ulceration. (3) Microangiopathy theory: it has been demonstrated that some of the capillaries in patients with venous non-healing wounds are caused by microthrombi or exhibit long intracapillary stasis. This in turn can reduce nutrition and oxygenation of the skin, predisposing to ulceration. [46]

Venous ulceration is a chronic disease, which is characterized by periods of exacerbation and remission. Venous non-healing wounds often take a long time to heal, which results in physical and psychological discomfort and negatively affects a patient's functional status. [28]

- **Arterial Non-healing wounds**

Arterial non-healing wounds occur as a result of reduced arterial blood flow and subsequent tissue perfusion.[47] Arterial or arteriolar chronic non-healing wounds due to any cause can result in ischemia of the skin and subcutaneous tissues which might lead to ulceration. Occur Peripheral vascular disease due to atherosclerosis, diabetes with microvascular or macrovascular disease, and/or vasculitis could lead to ischemic non- healing wounds resulting in ulceration.[46,47] A reduction in blood supply causes death of tissue in the area being fed by the affected artery. Ulcer development is often rapid with deep destruction of tissue. The limb looks pale, and there is a noticeable lack of hair.

There are three mechanisms involved in the pathophysiology of ischemic non-healing wounds: (1) extramural strangulation (2) mural thickening or accretion, and (3) intramural restriction of blood flow. There is often considerable overlap, and the exact pathogenesis cannot be always well defined. Most acute forms of vasculitis and some subacute and chronic forms are likely to cause non-healing wounds due to tissue hypoxia and exudation of fibrin-like substances. [25]

Arterial ulceration typically occurs over the toes, heels, and bony prominences of the foot. The ulcer appears "punched out" with well-demarcated edges and a pale, nongranulating, and necrotic base. [47]

Diabetic Foot non healing wounds

Diabetic foot non-healing wounds are common and estimated to affect 15% of all diabetic individuals during their lifetime. For instance, an estimated 18% of diabetic patients over the age of 65 in the US have non-healing foot non-healing wounds. [25] It is now appreciated that 15–20% of patients with such foot non-healing wounds go on to need an amputation. Almost 85% of the amputations are preceded by diabetic foot non-healing wounds.[48] Worldwide, it is estimated that a lower limb is lost every 30 seconds as a result of diabetic wound infection.[24]

Diabetic patients are at higher risk for arterial diseases and neuropathy, therefore, can develop non-healing wounds due to both entities. In addition, hyperglycaemia poses the risk of non-healing wounds secondary to neuropathic impairment of sensory, motor, and autonomic function, typically in the hand and foot, or "stocking and glove" distributions.[40] The etiology of diabetic foot non-healing wounds usually has many components. [49] The major underlying causes are noted to be peripheral neuropathy and ischemia from peripheral vascular disease. Other factors in ulceration are trauma, deformity, callus formation, and edema.[48,49]

- **Pressure wounds**

Pressure non-healing wounds are, as their name implies, caused primarily by unrelieved pressure. They usually occur over bony prominences such as the sacrum or the heel but can occur on any part of the body subjected to pressure. Approximately 70% of all pressure non-healing wounds occur in the geriatric population. Pressure non-healing wounds can be a major source of infection and lead to complications such as septicaemia,

osteomyelitis, and even death. Prevention of pressure damage to the skin and the underlying tissue is an essential part of treatment in at-risk patients. [18]

3. Management of Chronic Non-healing wounds

An ideal management plan for patients with chronic non-healing wounds should involve an early strategic and coordinated approach to delivering the correct treatment option for each individual patient, based on accurate assessment of the underlying pathophysiology

The management of non-healing wounds include a detailed history of the onset of the problem, examination of the legs and skin, investigations, and modalities of treatments. Successful management of non-healing wounds requires a clear diagnosis, establishment of a treatment plan, accurate monitoring, and adherence to the plan as the ulcer decreases in size. Education and training is vital for all those involved in caring for patients with chronic ulceration.[50]

Clinical Assessment

a. History

The first step toward diagnosis of any non-healing wounds ulcer is to compile a comprehensive history and assessment of the patient (Table 2). [51] This should in chronic

non-healing wounds include general health status, social and occupational situation, past and current medical history of relevant diseases (such as deep vein thrombosis, diabetes, autoimmune disorders, inflammatory bowel disease, and connective tissue disease), condition of the skin, current vascular status, limb size and shape, and history and status of the ulcer.[51] The patient should be asked about lower

extremity pain, paraesthesia, anaesthesia, and claudication. [40] It is important to determine the duration of ulceration and whether it is a first episode or recurrent. Pain is a major problem for patients with non-healing woundsnon-healing wounds unless there is a neuropathic component. Lack of pain, therefore, suggests a neuropathic aetiology. Patients should also be asked about their mobility.[39]

Table 2: Assessment of lower limb non-healing wounds[40,50]

Patient	History of ulcer development Past and current medical problems General health status Nutrition Social, occupation Mobility problem Limitations to self care Obesity
Skin changes	Arterial Malignant Autoimmune
Vascular assessment	Pedal pulses Ankle Brachial Pressure Index
Limb factors	Oedema Circumferences Lymphoedema Orthopaedic problems Sensation and pain
Ulcer	Site-venous, arterial, pressure Appearance Size-measure Wound base Exudate level Surrounding skin

Clinical course of the wound can suggest its etiology. Possible considerations to rule out in chronic non-healing wounds include diabetes; hypertension; hyperlipidaemia; coronary artery disease; alcohol and tobacco use; thyroid, pulmonary, renal, neurologic, and rheumatic diseases; peripheral vascular disease; deep vein thrombosis; specifically, cutaneous factors in chronic non-healing wounds

including cellulitis, trauma, and recent surgery.[40]

5.1.2. Examination

The examination of the non-healing wounds should include palpation of pulses and a search for the signs of venous hypertension, varicose veins, haemosiderin pigmentation, varicose eczema, atrophie blanche, and lipodermatosclerosis. The range of hip, knee, and ankle movement should be determined, and sensation should be tested to exclude a peripheral neuropathy. [39]

Examination should include chronic non-healing wounds site, size, appearance, wound base, exudates level, and surrounding skin (Table 2).[51] The surrounding region should be examined for pain, edema, erythema, warmth, induration, discoloration, maceration, dryness, scarring from previous wounds, hair pattern, gangrenous digits, chronic non-healing wounds, cyanosis, capillary refill, and varicose veins. It is important to bear in mind that venous and arterial disease may coexist in the same patient. [40]

The venous non-healing wounds considerably differ from arterial non-healing wounds (Table 3) [45] and other non-healing wounds of lower extremity (Table 4). [42] An irregular ulcer border, black necrosis, erythema, or bluish or purple discolorations of adjacent skin are suggestive for ulcer due to vasculitis. A painful non-healing wounds with violaceous borders suggests pyoderma gangrenosum.

Table 3: Common lower extremity non-healing wounds.[41,42]

Ulcer type	General characteristics	Pathophysiology	Clinical features
Venous	Most common type; women affected more than men; often occurs in older persons	Venous hypertension	Shallow, painful ulcer located over bony prominences, particularly the gaiter area (over medial malleolus); granulation tissue and fibrin present Associated findings include edema, venous dermatitis, varicosities, and lipodermatosclerosis
Arterial	Associated with cardiac or cerebrovascular disease; patients may present with claudication, impotence, and pain in distal foot; concomitant with venous disease in up to 25 percent of cases	Tissue ischemia	Ulcers are commonly deep, located over bony prominences, and round or punched out with sharply demarcated borders; yellow base or necrosis; exposure of tendons Associated findings include abnormal pedal pulses, cool limbs, femoral bruit, and prolonged venous filling time
Neuropathic	Most common cause of foot ulcers, usually from diabetes mellitus	Trauma, prolonged pressure	Usually occurs on plantar aspect of feet in patients with diabetes, neurologic disorders, or Hansen disease
Pressure	Usually occurs in patients with limited mobility	Tissue ischemia and necrosis secondary to prolonged pressure	Located over bony prominences; risk factors include excessive moisture and altered mental status

Investigations:

1. The Ankle Brachial Pressure Index (ABPI) using a handheld Doppler ultrasound and sphygmomanometer can be carried out for more accurate assessment of arterial perfusion. The results are used to determine the likelihood of arterial insufficiency and can be used to guide the management plan (Table 5).
   When Doppler tests indicate arterial insufficiency, arterial duplex ultrasonography will (noninvasively) provide accurate anatomic and haemodynamic information on the site and extent of the arterial disease. When indicated, further detailed anatomic information for treatment planning can be obtained from magnetic resonance angiography, computer tomographic angiography, or digital subtraction angiography.
2. Accurate and regular measurement of the wound is important to give an objective assessment of the effectiveness of the current management plan.
3. Blood investigations such as complete blood count, erythrocyte sedimentation rate, blood sugar, lipid profile, renal function tests, and liver function tests are essential in patients with chronic non-healing wounds. The plain radiography of the foot along with CT and MRI should be done to rule out osteomyelitis and malignancy.
4. Laboratory screening tests for vasculitis: urine analysis for proteinuria, hematuria, routine and immunohistopathology of skin biopsies, antinuclear antibodies, rheumatoid factor, complement C4, circulating immune complexes, paraproteins, immunoglobulin fractions, antineutrophil cytoplasmic antibodies, serological tests, and cultures for underlying infections.
5. Laboratory screening tests for clotting disorders: activated partial thromboplastin time, prothrombin time, thrombin time, factor V (Leiden) mutation (506R fi 506Q), factor II (prothrombin) mutation (20210G fi 20210A), antithrombin III, protein C and protein S, and lupus anticoagulant anticardiolipin.
6. Venography may be performed as an investigational procedure prior to valvular surgery. Lower extremities arteriography is indicated in patients with ischemic rest pain, intolerable claudication, impending gangrene, or the presence of nonhealing non-healing wounds of suspected arterial origin.
7. Colour duplex ultrasound scanning which is becoming the de facto standard for evaluation of venous obstruction is also used to assess the location and extent of reflux in venous non-healing wounds.
8. A quantitative bacterial culture is more specific and should be performed once wound infection is suspected. This is performed by curetting or biopsying the bed of the ulcer. The quantitative biopsy is the current gold standard for assessing the quality and quantity of microbial pathogens within wound. Quantitative biopsies containing greater than 10^5 organisms per gram of tissue are considered significant, and systemic antibiotic therapy should be considered. If osteomyelitis is suspected, representative cultures need to be obtained from the bone or deepest tissue layers.
9. Ulcer biopsy is important in making a correct diagnosis and to rule out malignancy as these non-healing wounds are prone to malignant transformation. This requires taking a deep wedge of tissue from the ulcer edge and can usually be performed under local anaesthesia. Chronic non-healing wounds are sometimes biopsied for experimental protocols: (A) to obtain information regarding the wound bed or the wound edge. (B) to grow cells in vitro from nonhealing wound.

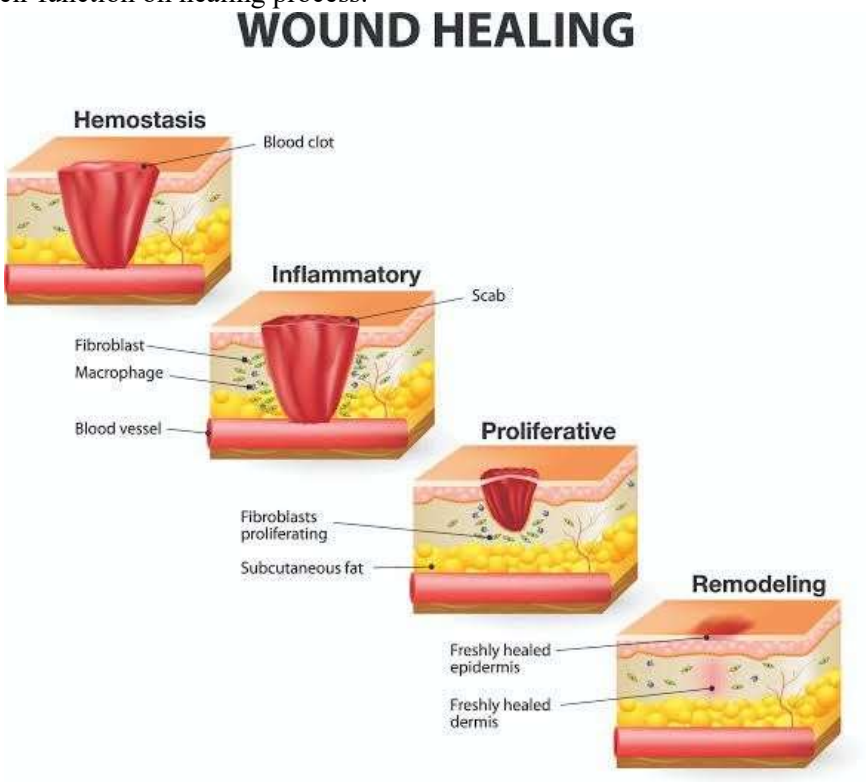
4. Healing and factors affecting wound/ulcer healing process[52]

A wound is defined as a disruption in the continuity of the epithelial lining of the skin or mucosa resulting from physical or thermal damage. According to the duration and nature of healing process, the

wound is categorised as acute and chronic. An acute wound is an injury to the skin that occurs suddenly due to accident or surgical injury. It heals at a predictable and expected time frame usually within 8-12 weeks depending on the size, depth and the extent of damage in the epidermis and dermis layer of the skin. Chronic wounds on the other hand fail to progress through the normal stages of healing and cannot be repaired in an orderly and timely manner.

Chronic wounds generally result from decubitis ulcer, non-healing wounds and burns. Wound healing is a dynamic and complex process of tissue regeneration and growth progress through four different phases

1. the coagulation and haemostasis phase (immediately after injury);
2. the inflammatory phase, (shortly after injury to tissue) during which swelling takes place;
3. (iii) the proliferation period, where new tissues and blood vessels are formed and
4. the maturation phase, in which remodelling of new tissues takes place. These phases occur in an ordered manner overlapping with each other in a well- connected cascade. Promotion of these phases are largely depending on the wound type and its associated pathological conditions and the type of dressing material. With the advancement in technology, currently, different types of wound dressing materials are available for all types of wounds. But the selection of a material for a particular wound is important to achieve faster healing. In this review, an attempt has been made to consolidate the different types of wound dressing materials and their function on healing process.



Factors affecting wound healing process[52]

Wound healing is the result of interactions among cytokines, growth factors, blood and the extracellular matrix. The cytokines promote healing by various pathways such as stimulating the production of components of the basement membrane, preventing dehydration, increasing inflammation and the formation of granulation tissue. These pathways are affected by various local and systemic factors. Local factors which include chronic non-healing wounds pain, infection, radiation and tissue oxygen

tension directly influence the characteristics of the wound whereas systemic factors are the overall health or disease state of the individual that affect individual's ability to heal. In addition to these factors, poor nutrition, age and protein, vitamins and mineral deficiency can also prolong healing times.

- **Syndromes associated with abnormal healing**

Ehlers-Danlos syndrome (EDS) is a genetic connective tissue disorder characterized by defects of the major structural protein Collagen. Autosomal dominant and autosomal recessive forms of EDS equally affect males and females. Since the collagen is a major structural protein and provide elasticity to body cells and tissues, its damage results in articular hyper mobility leading to partial or complete dislocation of joints and elastic skin. Based on the defects and inheritance mode, EDS is categorised into six major subtypes and they are distinct in affecting individuals.[53]

Cutis Laxa is characterised by (Lysyl oxidase) enzyme deficiency resulting in abnormality of copper metabolism leads to abnormal loose skin, muscular organ and skeletal abnormality. Wrinkled skin, particularly on the neck and mild mental retardation also characterised by this disorder. X-linked cutis laxa also called as (OHS) occipital horn syndrome, a rare disorder that was formely classified as a subtype of EDS. Cutis laxa is further classified into four genetic forms based on their pattern of inheritance. These inchronic non-healing woundsdes sex-linked defective on X chromosome, autosomal dominant defective on autosomal chromosome and two types of autosomal recessive
inheritance defective on chromosome 5 Among these types, autosomal recessive forms are more severe than other forms. [54]

- **Characteristics of an ideal wound dressing**

Based on the wound type, suitable dressing material must be used. Dressing selection should be based on its ability to a) provide or maintain moist environment b) enhance epidermal migration c) promote angiogenesis and connective tissue synthesis d) allow gas exchange between wounded tissue and environment e) maintain appropriate tissue temperature to improve the blood flow to the wound bed and enhances epidermal migration f) provide protection against bacterial infection and g) should be non-adherent to the wound and easy to remove after healing h) must provide debridement action to enhance leucocytes migration and support the accumulation of enzyme and i) must be sterile, non-toxic and non-allergic.

5. Wound Dressings

Wound, whether it is a minor cut or a major incision, it is important to care for it properly, part of this process in chronic non-healing wounds is wound dressing. Dressing is designed to be in contact with the wound, which is different from a bandage that holds the dressing in place. Historically, wet-to-dry dressings have been used extensively for wounds requiring debridement. In 1600 BC, Linen strips soaked in oil or grease covered with plasters was used to cover chronic non-healing wounds. Clay tablets were used for the treatment of wounds by Mesopotamian origin from about 2500 BCE. They cleaned wounds with water or milk prior to dressing with honey or resin. Wine or vinegar usage for cleaning the wounds with honey, oil and wine as further treatment was followed by Hippocrates of ancient Greece in 460- 370 BCE. They used wool boiled in water or wine as a bandage.[55] There was a major breakthrough in the antiseptic technique during the 19th century, antibiotics were introduced to control

infections and decrease mortality. Modern wound dressing arrival was in 20th century. [56]
When the wound is closed with dressing they are continuously exposed to proteinases, chemotactic, complement & growth factors, which is lost in the wound exposed. So during late 20th century, production of chronic non-healing wounds dressing began to protect and provide moist environment to wound. These dressings helps in faster re- epithelialisation, collagen synthesis, promotes angiogenesis by creating hypoxia to the wound bed and decreases wound bed pH which leads to decrease in the wound infection. [56] Woven absorbent cotton gauze was used in 1891. Until the mid-1900's, it was firmly believed that wounds healed more quickly if kept dry and uncovered whereas 'closed wounds heal more quickly than open wound' written in an Egyptian medical text -Edwin smith surgical papyrus in 1615 BC. Oscar Gilje in 1948 describes moist chamber effect for healing non-healing wounds. In the mid 1980's, the first modern wound dressing were introduced which delivered important characteristics providing moisture and absorbing fluids (e.g. polyurethane foams, hydrocolloids, iodine-containing gels). During the mid- 1990's, synthetic wound dressings expanded into various group of products which include chronic non-healing wound hydrogels, hydrocolloids, alginates, synthetic foam dressing, silicone meshes, tissue adhesives, vapor-permeable adhesive films and silver/collagen containing dressing.

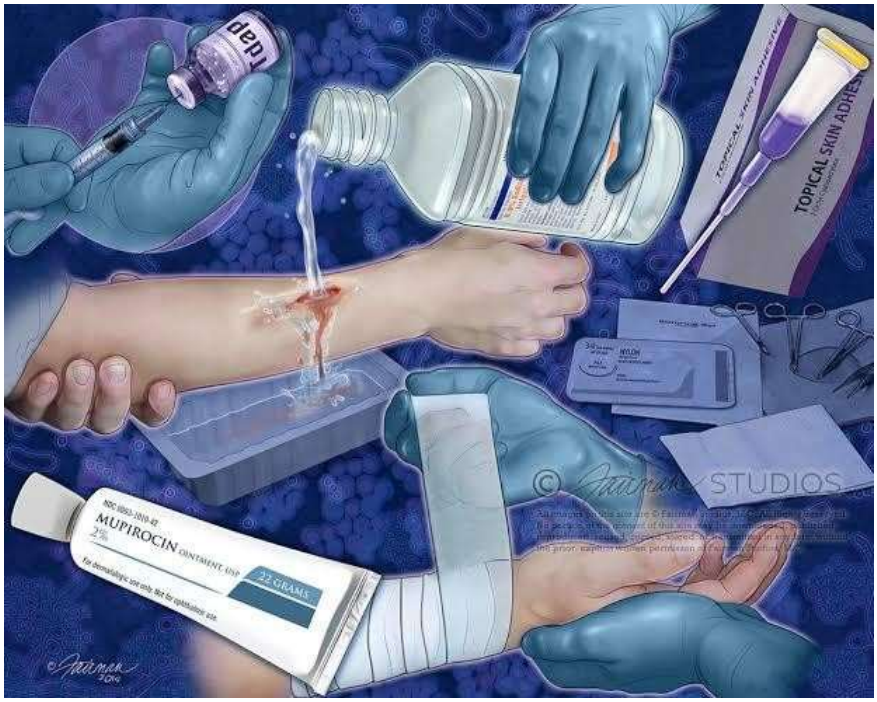
- **Traditional wound dressing[52]**

Traditional wound dressing products in chronic non-healing wounds including gauze, lint, plasters, bandages (natural or synthetic) and cotton wool are dry and used as primary or secondary dressings for protecting the wound from contaminations. Gauze dressings made out of woven and non-woven fibres of cotton, rayon, polyesters afford some sort of protection against bacterial infection. Some sterile gauze pads are used for absorbing exudates and fluid in an open wound with the help of fibres in these dressings. These dressings require frequent changing to protect from maceration of healthy tissues. Gauze dressings are less cost effective. Due to excessive wound drainage, dressings become moistened and tend to become adherent to the wound making it painful when removing. Bandages made out of natural

cotton wool and cellulose or synthetic bandages made out of polyamide materials perform different functions. For instance, cotton bandages are used for retention of light dressings, high compression bandages and short stretch

compression bandages provide sustained compression in case of venous non-healing wounds. Xeroform™ (non-chronic non-healing wounds dressing) is petrolatum gauze with 3% of Bismuth tribromophenate used for non-exudating to slight exudating wounds. Tulle dressings such as Bactigras, Jelonet, Paratulle are some examples of tulle dressings commercially available as impregnated dressings with paraffin and suitable for superficial clean wound. Generally traditional dressings are indicated for the clean and dry wounds with mild exudate levels or used as secondary dressings. Since traditional dressings fail to provide moist environment to the wound they have been replaced by modern dressings with more advanced formulations.

- **Modern wound dressing**



Modern wound dressing have been developed to facilitate the function of the wound rather than just to cover it. These dressings are focused to keep the wound from dehydration and promote healing. Based on the cause and type of wound, numerous products are available in the market, making the selection a very difficult task. Modern wound dressings are usually based on synthetic polymers and are classified as passive, interactive and bioactive products.

Passive products are chronic non-healing wounds such as gauze and tulle dressings, used to cover the wound to restore its function underneath. Interactive dressings are chronic non-healing wounds available in the forms of films, foam, hydrogel and hydrocolloids. These dressings act as a barrier against penetration of bacteria to the wound environment. **57-60**

- **Semi-permeable film dressings[52]**

These dressings are composed of transparent and adherent polyurethane which permits transmission of water vapour, O2 and CO2 from the wound and it also provides autolytic debridement of eschar and impermeable to bacteria. Initially, films were made from nylon derivatives with an adhesive polyethylene

frame as the support which made them chronic non-healing wounds. Originally nylon derived film dressings were not used for highly exudating wounds due to their limited absorption capacity and caused maceration of the wound and the healthy tissues around the wound. But, these dressings are highly elastic and flexible, and can conform to any shape and do not require additional tapping. Inspection of wound closure is also possible without removal of wound dressing because of transparent films. Hence these dressings are recommended for epithelializing wound, superficial wound and shallow wound with low exudates, e.g. Opsite™, Tegaderm™, Bioochronic non-healing woundssive™. Commercially available film dressings differ in terms of their vapour permeability, adhesive characteristics, conformability and extensibility.

- **Semi-permeable foam dressings**[52]

Foam dressings are made up of hydrophobic and hydrophilic foam with adhesive borders sometimes. The hydrophobic properties of outer layer protect from the liquid but allow gaseous exchange and water vapour. Silicone-based rubber foam (silastic) molds and contours to wound shape. Foam has capability of absorbing varying quantities of wound drainage depending upon the wound thickness. Adhesive and non-adhesive foam dressings are available. Foam dressings are suitable for lower non-healing wounds and moderate to highly exudating wounds, also indicated for granulating wounds. They are generally used as primary dressings for absorption and secondary dressings are not required due to their high absorbency and moisture vapour permeability. Disadvantage of foam dressing is requiring frequent dressing and is not suitable for low exudating wounds, dry wounds and dry scars as they depend on exudates for its healing e.g. Lyofoam™, Allevyn™ and Tielle™.

Hydrogels dressing

Hydrogels are insoluble hydrophilic materials made from synthetic polymers such as poly (methacrylates) and polyvinyl pyrrolidine. The high-water content of hydrogels (70-90 %) helps granulation tissues and epithelium in a moist environment. Soft elastic property of hydrogels provides easy application and removal after wound is healed without any damage. Temperature of cutaneous wounds is decreased by hydrogels providing soothing and cooling effect. Hydrogels are used for dry chronic wounds, necrotic wounds, pressure non-healing wounds and burn wounds. Morgan[61] has reported that except infected and heavy drainage wounds, hydrogel dressings are suitable for all four stages of wound healing. Hydrogel dressings are non-irritant, non-reactive with biological tissue and permeable to metabolites. Many researchers have reported that hydrogel dressings are used to treat chronic non-healing wounds. Difficulties of hydrogel dressings are exudate accumulation leads to maceration and bacterial proliferation that produces foul smell in wounds. Besides, low mechanical strength of hydrogels making it difficult to handle. [62] Some examples of hydrogels are Intrasite™, Nu-gel™, Aquaform™ polymers, sheet dressings, impregnated gauze and water-based gels.

- **Hydrocolloid dressing**

Hydrocolloid dressings are among the most widely used interactive dressings and are consist of two layers, inner colloidal layer and outer water- impermeable layer. These dressings are made up of the combination of gel forming agents (carboxymethylcellulose, gelatin and pectin) with other materials such as elastomers and adhesives. [63] Hydrocolloids are permeable to water vapor but impermeable to bacteria

and also have the properties of debridement and absorb wound exudates. [63] They are used on light to moderately exudating wounds such as pressure sores, minor burn wounds and traumatic wounds. These dressings are also recommended for paediatric wound care management, as they do not cause pain on removal. [63] When these hydrocolloids contact with the wound exudate, they form gels and provide moist environment that helps in protection of granulation tissue by absorbing and retaining exudates. Granuflex™, Comfeel™, Tegasorb™ are available in the form of sheets or thin films. Disadvantage of hydrocolloids are they are not indicated for neuropathic non-healing wounds or highly exudating wounds, also they are mostly used as a secondary dressing. [63]

- **Bioactive wound dressings**

The last type of modern wound dressing is bioactive dressings and is produced from biomaterials which play an important role in healing process. These dressings are known for their biocompatibility, biodegradability and non-toxic nature and are derived generally from natural tissues or artificial sources [65] such as collagen [66], hyaluronic acid[67], chitosan[68], alginate and elastin. Polymers of these materials are used alone or in combination depending on the nature and type of wound. Biological dressings are sometimes incorporated with growth factors and antimicrobials to enhance wound healing process.

Collagen, a major structural protein has been discussed by many researchers for their active role in natural healing process. [69] Collagen initiates fibroblast formation and accelerates endothelial migration upon contact with wound tissue. [70] Hyaluronic acid (HA) is a glycoaminoglycan component of extra cellular matrix (ECM) with unique biological and physicochemical features. Similar to collagen, HA also biocompatible, biodegradable and lack immunogenicity naturally. [71] Chitosan promotes the formation of granulation tissue during the proliferative stage of wound healing. [72,73,74] When compared to other dressings, biological dressings are reported to be more superior to other types of dressings.

- **Composite dressing[52]**

Composite dressings are versatile and convenient for both partial and full thickness wounds. A composite or combination dressings has multiple layers and each layer is physiologically distinct. Most of the composite dressings possess three layers. Composite dressings may also in chronic non-healing wounds include an adhesive border of non- woven fabric tape or transparent film. They can function as either a primary or a secondary dressing on a wide variety of wounds and may be used with topical medications. Outer most layer protect the wound from infection, middle layer usually composed of absorptive material which maintains moisture environment and assist autolytic debridement, bottom layer composed of non-adherent material which prevents from sticking to young granulating tissues. Composite dressings have less flexibility and they are more expensive.

Role of homey in management of chronic non-healing wounds

HEALING PROPERTIES OF HONEY

Honey has long been documented as having healing properties.[75,76,77] Honey and sugar paste were associated with scarless healing in cavity wounds. It has been reported that rabbit wounds treated with a topical application of honey showed less edema, fewer polymorphonuclear and mononuclear cell infiltrations, less necrosis, better wound contraction, improved epithelialization, and lower

glycosaminoglycan and proteoglycan concentration. [78,79,80,81,82,83] Furthermore, honey causes significantly greater wound contraction than controls, and it promotes the formation of granulation tissue and epithelialization of wounds. Honey stimulates tissue growth, synthesis of collagen, and development of new blood vessels in the bed of wounds. Intraperitoneal honey administration after an adhesion model in the cecum and terminal ileum of rats reduced postoperative adhesion. [84,85,86,87,88]

HONEY AND WOUNDS

Generally, wound healing can be affected by endogenous (pathophysiology) and exogenous (microorganisms) factors. The risk of wound infection increases as local conditions favour bacterial invasion and growth. Therefore, microbial colonisation of both acute and chronic wounds is inevitable. Many species of bacteria have been recovered from wounds, but *Staphylococcus aureus* is the most frequently isolated from wound pathogens [45]. In addition, *Pseudomonas aeruginosa* is an important pathogen in chronic wounds and burns; its presence has been demonstrated in numerous studies and has been found in one third of chronic non-healing wounds.

Infection with *S. aureus* and pseudomonads retards ulcer healing rates and, with pseudomonads and B-hemolytic streptococcus, reduces the success of skin grafts used for non-healing wounds. The widespread development of antibiotic-resistant bacteria is a challenging problem. Therefore, current interest is focused on an alternative to antibiotics and conventional therapies, such as honey, antimicrobial moisture-retentive dressings, essential oils and cationic peptides, topical enzymes, biosurgical therapies, and vacuum therapies. In addition, unregulated inflammation caused by both microorganisms and underlying abnormal pathophysiological conditions is a major factor associated with the process of healing in chronic wounds. Many research works reported the use of honey for treatment of both wounds and infections.

Table 5 summarises many papers that reported successful use of honey in wound healing. Honey with proven antibacterial activity has the potential to be an effective treatment option for wounds infected or at risk of infection with various human pathogens. The medical literature on treating wounds with honey has been reviewed. As a dressing on wounds, honey provides a moist healing environment, rapidly clears infection, deodorizes, and reduces inflammation, edema, and exudation. It increases the rate of healing by stimulation of angiogenesis, granulation, and epithelialization.

Table 4: Effects of Honey on Wounds Healing[89]

Origin of Honey	Type of Lesion	Effects of Honey
Iran[31]	Surgical incision on rabbits	Less edema, fewer polymorphonuclear and mononuclear cell infiltrations, less necrosis, better wound contraction, improved epithelialization, and lower glycosaminoglycan and proteoglycan concentrations
India[39]	Wounds created on buffalo calves	Promotes granulation and scar formation, complete healing of full-thickness wounds occurred faster with honey than with nitrofurazone or sterilized petrolatum
India[40]	Wounds created on buffalo calves infected with *S. aureus*	Faster rate of healing compared with ampicillin ointment and saline treatments, the least inflammation, the most rapid fibroblastic and angioblastic activity and epithelialization
India[42]	Full-thickness skin wounds made on back of rats	Increases significantly the quantity of collagen synthesized and degree of cross-linking of the collagen in the granulation tissue
Egypt[64]	Infected diabetic foot wounds	Fast healing and significant decrease of bacterial load
Turkey[65]	Split-thickness skin graft donor site	Wounds show faster epithelialization time and a low sense of pain than paraffin gauzes and saline-soaked gauzes
Turkey[44]	An adhesion model constituted in the cecum and terminal ileum of rats	Intraperitoneal honey administration reduces postoperative peritoneal adhesion
Turkey[66]	Intraurethral injury in rats	Prevents inflammation, accelerates urethral healing, and provides perfect healing
United Arab Emirates[67]	Injured skin or conjunctiva in mice or rat	Accelerates wound healing and eradicates infection
Yemen[68]	Postoperative wound	Eradicates bacterial infection, accelerates wound healing, and minimizes scar formation
Thailand[69]	Postoperative wound disruption	Complete wound healing within 2 weeks
Nepal[71]	Radiation-induced oral mucositis	Strongly protective against the development of mucositis
Nigeria[72]	Wounds and ulcers	Debrides wounds rapidly, replacing sloughs with granulation tissue, promotes rapid epithelialization, and absorption of edema
Nigeria[73]	Fournier's gangrene	Accelerates wound healing
Mexico[33]	Fournier's gangrene	Accelerates wound healing
Malawi[76]	Patients with open or infected wounds	More effective than sugar in reducing bacterial contamination and promoting wound healing
Norway[80]	Chronic wound infection	Eradicates wound bacterial infections and penetrates biofilm
Ireland[81]	Nonhealing ulcers	Manuka honey decreases wound pH and causes a reduction in wound size
France[82]	Wounds	Accelerates wound healing
Germany[84]	Resistant wound infection in seven patients	Complete wound healing
U.K.[85]	Toenail surgery	Partial avulsion wounds healed faster with paraffin tulle gras than with the honey dressing
U.K.[88]	Chronic wounds	Clinical benefits from using honey in wound care
U.K.[89]	Meningococcal skin lesions	Helps skin healing
Netherlands[91]	Sixty patients with chronic wounds	Honey is easy to apply, helpful in cleaning the wounds, and without side effects

Table 5: demonstrates general effects of honey on the healing process[89]

1.	Causes greater wound contraction[31,32,33,34,35,36,37,211])
2.	Promotes the formation of granulation tissue[32,33,34,35,36,37,39,92]
3.	Promotes epithelialization of wounds[32,33,34,35,36,37,66,73,92]
4.	Stimulates tissue growth, synthesis of collagen[38,39,40,41,42,43,92]
5.	Stimulates development of new blood vessels in the bed of wounds[38,39,40,41,42,43,62,93]
6.	Reduces postoperative adhesion[44]
7.	Reduces edema[62,73,92,93]
8.	Reduces inflammation[61,62,68,92,93,119]
9.	Deodorizes wounds[62,92,93]
10.	Promotes moist wound healing[61,92]
11.	Facilitates debridement[61,72,93]
12.	Reduces pain[66,84,92]

6. Studies conducted in the past on similar topic

Molan[90] published a review article that covered the various reports that have been published on the clinical usage of honey. Positive findings on honey in wound care have been reported from 17 randomized controlled trials (1965 patients) and five clinical trials of other forms (97 patients) treated with honey. On experimental animals, the effectiveness of honey in assisting wound healing has also been demonstrated in 16 trials. There is also a large amount of evidence in the form of case studies.

In a recent review aimed to determine whether honey increases the rate of healing in acute wounds (burns, lacerations, other traumatic wounds) and chronic wounds (venous non-healing wounds, arterial non-healing wounds, diabetic non-healing wounds, pressure non-healing wounds, infected surgical wounds), 19 trials (n = 2554) were identified. chronic non-healing, honey may improve healing times in mild to moderate superficial and partial-thickness burns compared with some conventional dressings. However, honey dressings as an adjuvant to compression do not significantly increase non-healing wounds-ulcer healing at 12 weeks. [91]

Another article provides an overview of the use of honey in wound management and reviews the evidence to support its effectiveness in the management of wound healing. Honey has anti-inflammatory and antibacterial effects without antibiotic resistance; it promotes moist wound healing and facilitates debridement. A summary of the current evidence base for the use of honey, a review of its therapeutic effects, and a discussion of the implications for WOC nursing practice was published recently. In the U.S., a honey product received FDA approval in 2007. [92]

In India, a study showed that granulation, scar formation, and complete healing of full- thickness wounds created on buffalo calves occurred faster with honey than with nitrofurazone or sterilised petrolatum.[88]

In another study, full-thickness skin wounds were made on buffalo calves after infecting the wound by subcutaneous injections of *S. aureus* 2 days prior to wounding. Topical application of honey, ampicillin ointment, and saline were compared. Honey gave a faster rate of healing compared with ampicillin

ointment and saline treatments, the least inflammation, the most rapid fibroblastic and angioblastic activity, and epithelialisation. [93]

Full-thickness skin wounds made on the backs of rats were treated with topical application of honey to the wound, oral administration of honey, or intraperitoneal administration of honey. Honey increased significantly the quantity of collagen synthesised and degree of cross-linking of the collagen in the granulation tissue. Systemic treatment gave greater increase than topical treatment, while the intraperitoneal route produced better results than the oral route. The thickness of granulation tissue and the distance of epithelialisation from the edge of the wound were significantly greater and the area of the wound significantly smaller in wounds treated with honey compared with control when honey was applied on excising skin on the mice down to muscles. [94]

In Egypt, 30 infected diabetic foot wounds were randomly selected for treatment with clover honey. The honey dressing was applied to wounds for 3 months until healing, grafting, or failure of treatment. Results showed that complete healing was significantly achieved in 43.3% of non-healing wounds, and decrease in size and healthy granulation was significantly observed in another 43.3% of patients. After 1- week, bacterial load of all non-healing wounds was significantly reduced. The authors reported that commercial clover honey is a clinical and cost-effective dressing for diabetic wounds in developing countries. [95]

From Turkey, for the treatment of a split-thickness skin graft donor site, honey- impregnated gauze showed faster epithelialization time and a lower sense of pain than paraffin gauzes and saline-soaked gauzes. [96]

In Israel, nine infants with large, open, infected wounds that failed to heal with conventional treatment were treated with honey. All infants showed marked clinical improvement after 5 days of treatment with topical application of 5–10 ml of honey twice daily. [97]

Another study from Nepal investigated whether honey's anti-inflammatory properties might limit the severity of radiation-induced oral mucositis. A single-blinded, randomized, controlled clinical trial was carried out to compare the mucositis-limiting qualities of honey with lignocaine. It was found that honey is strongly protective against the development of mucositis. The authors conchronic non-healing woundsded that honey applied topically to the oral mucosa of patients undergoing radiation therapy appears to provide a considerable benefit by limiting the severity of mucositis. [98]

In Nigeria, 59 patients with wounds and non-healing wounds, most of which had failed to heal with conventional treatment, were treated with unprocessed honey. Fifty-eight cases showed remarkable improvement following topical application of honey. Honey debrided wounds rapidly, replacing sloughs with granulation tissue. It also promoted rapid epithelialization and absorption of edema from around the ulcer margins. [99]

HONEY AND SKIN NON-HEALING WOUNDS

Honey has been used in the treatment of non-healing wounds due to various etiologies.

In a review of the literature, more than 470 cases were treated with honey; there were only five cases where successful healing was not achieved [102]. [100]

In another review study, the authors summarised evidence of honey's effectiveness, its hypothesised

mechanism of action, potential risks and benefits, the types of honey available, and the nature of its application. Critical aspects of ulcer care are also reviewed. It was -chronic non-healing wound that honey is a low-cost topical therapy with important potential for healing [103]. **101**

The use of honey in two patients with pressure non-healing wounds resulted in a rapid and complete healing of both wounds. The antibacterial activity of honey had a deodorising effect on the wounds and its anti-inflammatory actions reduced the level of pain. Further, honey was used successfully for necrotising breast ulcer management.**102** Out of 59 treated patients with wounds and non-healing wounds, 58 patients showed remarkable improvement following topical application of honey; sloughs, necrotic, and gangrenous tissue separated and could thus be lifted off painlessly. **102**

Materials and Methods

Study setting: General Surgery OPD and ward at Tertiary Health Centre

Study population: All the patient with clinically diagnosed chronic non healing ulcers and wounds

Study period: 24 months (October 2019 to october2021)

Study design: Prospective experimental interventional hospital based comparative study

Sample size:

Formula for sample size calculation

(Source: Lwanga SK, Lameshaw S. Sample size determination in health studies WHO, Geneva, 1991) **103**

$$n = \frac{\{z1\sqrt{[2P(1-P)]} + z2\sqrt{[P1(1-P1) + P2(1-P2)]}\}^2}{(P1-P2)^2}$$

Ref article:

Gulati S, Qureshi A, Srivastava A, Kataria K, KumarP, BalakrishnaJi A. A prospective randomized study to compare the effectiveness of honey dressings vs. povidone iodine dressing in chronic wound healing. Indian J Surg 2014; 76(3): 193–198.**104**

Variable used for sample size calculation: Incidence of wound healing between two groups is considered here for sample size calculation

P1	Probability of variable in sample-1 (Value <1.0)	0.8
P2	Probability of variable in sample-2 (Value <1.0)	0.6
P	Arithmetic average of P1 & P2	0.7
AH	Alternate hypothesis ONE sided (1), or TWO sided? (2)	1
1-α	Set level of confidence (value<1.0). Usual values 0.95;0.99	0.95
1-β	Set level of power of test (value<1.0). Usual values 0.8;0.9	0.8
Z1	Z value associated with set level of alpha (One sided)	1.64

Z2	Z value associated with set level of beta	0.84
n1	**Minimum sample size**	**50**

By using above formula and putting the values in it, minimum sample size came to 50 in each group. So our total sample size is 100
Sampling technique: Simple random sampling method

Inclusion criteria:
- Chronic non diabetic non healing wounds
- Superficial and deep burns wounds
- Chronic venous ulcer

Exclusion criteria:
- Diabetic non healing wounds
- Wet gangrene

Variables used in study: Age, gender, ulcer type, duration of healing, duration of hospitalization, granulation tissue, pain etc.

Methods of data collection:
Primary source data will be collected from a specially designed case recording proforma (CRF) pertaining to the selected patients, after explaining the options of treatment to each of the patient in the language understood by them and taking their consent will be subjected to a detailed history elicitation followed by thorough clinical examination. They will then be subjected for detailed clinical examination with baseline Investigations, posted for surgical procedures if required & Follow up of patients during hospital stay will be done. All the procedures investigations will be conducted under direct guidance and supervision of my guide.

Pretherapy Assessment
All patients were assessed by a consultant surgeon. Patients suffering from leg or foot ulcer were evaluated with color duplex scan to assess the arterial/ venous insufficiency. An X-ray of the region was also carried out to rule out any underlying osteomyelitis. A wound bacterial culture swab was collected before inclusion in the study. Washout period of 1 week was given to all the subjects before randomization. During 1 week of washout period, chronic wounds were cleansed with sterile normal saline (0.9 %) and covered with sterile paraffin gauze, cotton pads, and bandages.

Methods of Wound Care
Computer-generated random numbers using block randomization were used to develop the randomization schedule. The subjects were randomized into two groups—the honey dressing group and the povidone iodine dressing group—with the help of numbered opaque sealed envelopes. The honey was prepared by experienced ayurvedacharya of Patanjali Yogpeeth, Haridwar, by collecting it from a beehive on a neem tree (Azadericta indica). In the ayurvedic text, this honey is regarded as having

special wound-healing property.

The honey was sterilized by gamma-irradiation and was applied on 23 wounds in the experimental group. Ten percent povidone iodine solution was applied on 22 wounds. The wound surface was cleansed with normal saline followed by application of honey or povidone iodine (1–2 ml), just sufficient to fill the wound cavity. The wound was covered with a transparent sterile polyurethane semipermeable membrane sheet (Tegaderm 3M, USA) (Fig. 1). The Tegaderm sheet served as an occlusive dressing and retained the honey or povidone iodine in the wound cavity. The wound dressings were changed on alternate days for 6 weeks of follow-up period or till complete healing. Dressing in patients suffering from venous leg ulcer was reinforced by elastic compression garments.

The observations of wound healing status were made at 2-week intervals at second, fourth, and sixth weeks. Wound swab for bacteriological culture was taken at each visit.

The pain and overall comfort were recorded on a visual analog scale (VAS). Wound tracings were made on a transparent acetate sheet on each visit. From these tracings wound surface area (in cm2) was determined by computer image analysis with software package IMAGE-Pro plus (version 4.1). An adverse reaction form was filled in to record adverse reaction to povidone iodine or honey on each visit.

Outcome Variable

The main outcome of interest was complete healing at the end of the sixth week. Secondary outcomes were reduction in wound surface area measured in cm2, pain during dressing change measured on a VAS of 0–10 (0 meaning no pain and 10 indicating very severe pain), and overall comfort of subjects with dressing measured on the VAS of 0– 10 (0 indicating no comfort and 10 indicating maximum comfort).

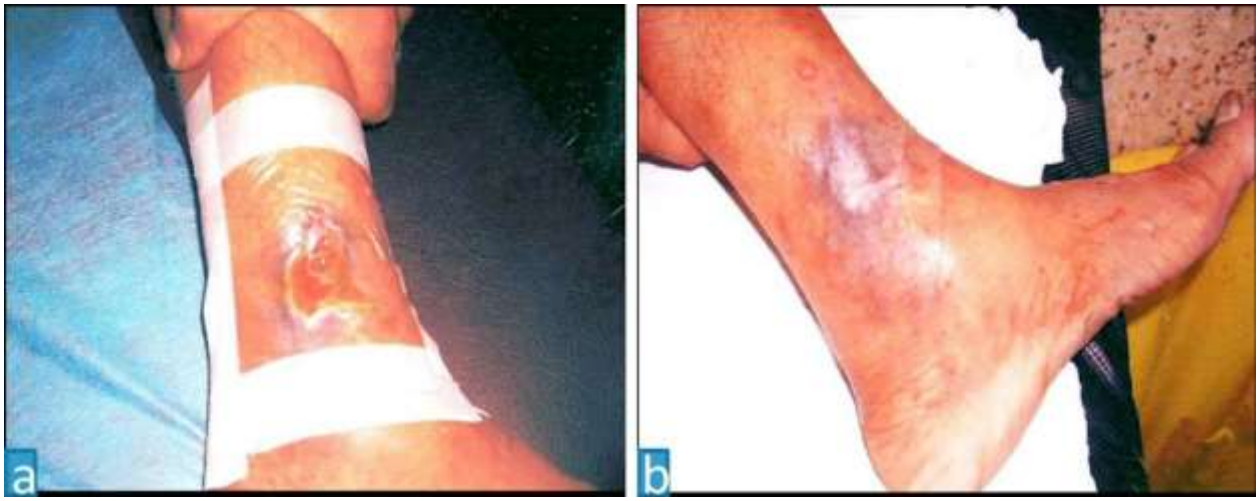


Figure 1: (a) Transparent sterile polyurethane occlusive dressing for retaining honey in the wound cavity and (b) complete healing of wound after 6 weeks of honey dressing

Statistical analysis and methods-

Data will be collected by using a structure proforma. Data entered in MS excel sheet and analysed by using SPSS IBM USA.

Qualitative data will be expressed in terms of proportions

Quantitative data will be expressed in terms of Mean and Standard deviation

Comparison of mean and SD between two groups will be done by using unpaired t test to assess whether

the mean difference between groups is significant or not
Descriptive statistics of each variable will be presented in terms of Mean, standard deviation, standard error of mean.
Association between two qualitative variables will be seen by using Chi square/ Fischers exact test
A p value of <0.05 will be considered as statistically significant whereas a p value <0.001 will be considered as highly significant.

Results

Table 1: Distribution according to age group

		Honey		Conventional dressing		Total
		No	%	No	%	
Age group in years	1 to 20	6	12.0	6	12.0	12
	21 to 40	7	14.0	7	14.0	14
	41 to 60	22	44.0	22	44.0	44
	61 to 80	15	30.0	15	30.0	30
Total		50	100.0	50	100.0	100

We included total 50 chronic non diabetic non healing wounds in two groups. One groups of wounds was treated with honey and other group was treated with conventional dressing. We matched age groups in both the treatment groups. Majority of the patients
i.e. 22(44%) were from 41-60 years age group in both groups, followed by 15(30%) from 61-80 years, 7(14%) from 21-40 years and least i.e. 6(12%) from 1-20 years age group.

Fig 1: Bar diagram showing Distribution according to age group

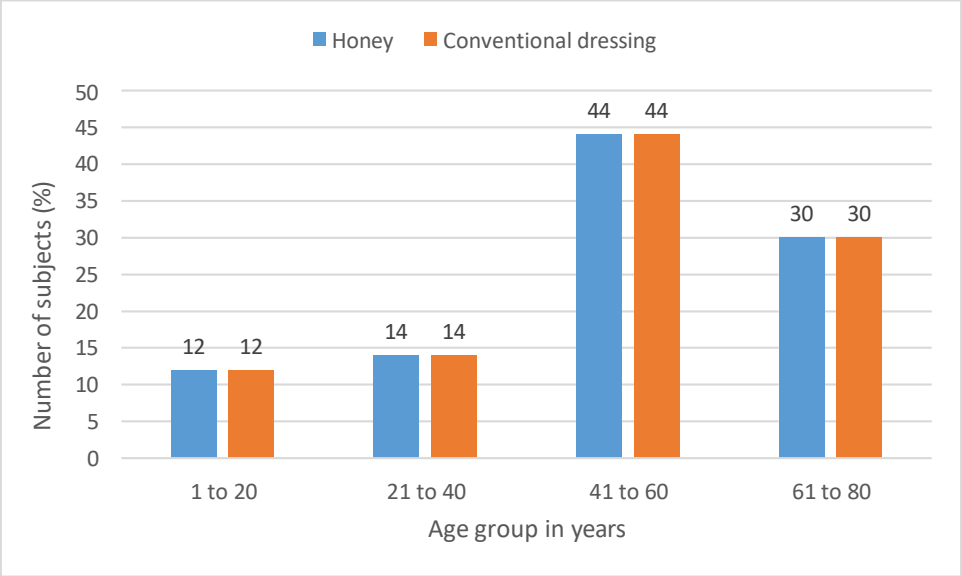


Table 2: Distribution according to gender

		Honey		Conventional dressing		Total
		No	%	No	%	
Gender	Female	19	38.0	19	38.0	36
	Male	31	62.0	31	62.0	60
Total		50	100.0	50	100.0	100

We matched gender in both the treatment groups. Accordingly, 62% were males and 38% were females in both the groups.

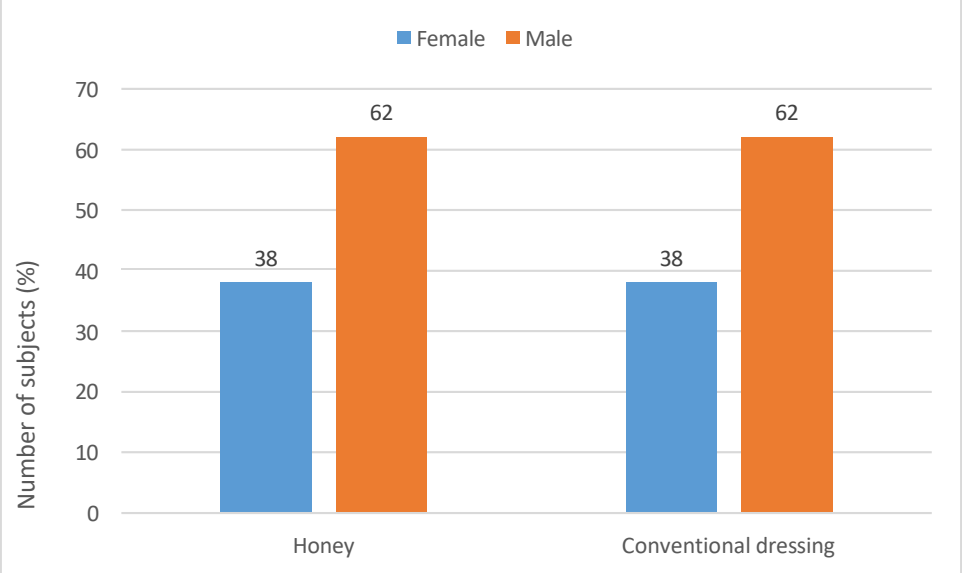


Fig 2: Bar diagram showing Distribution according to gender

Table 3: Distribution according to place of residence

		Honey		Conventional dressing		Total
		No	%	No	%	
Urban/Rural	Rural	39	78.0	39	78.0	78
	Urban	11	22.0	11	22.0	22
Total		50	100.0	50	100.0	100

78% of patients in both the group were from rural area whereas 22% were from urban area.

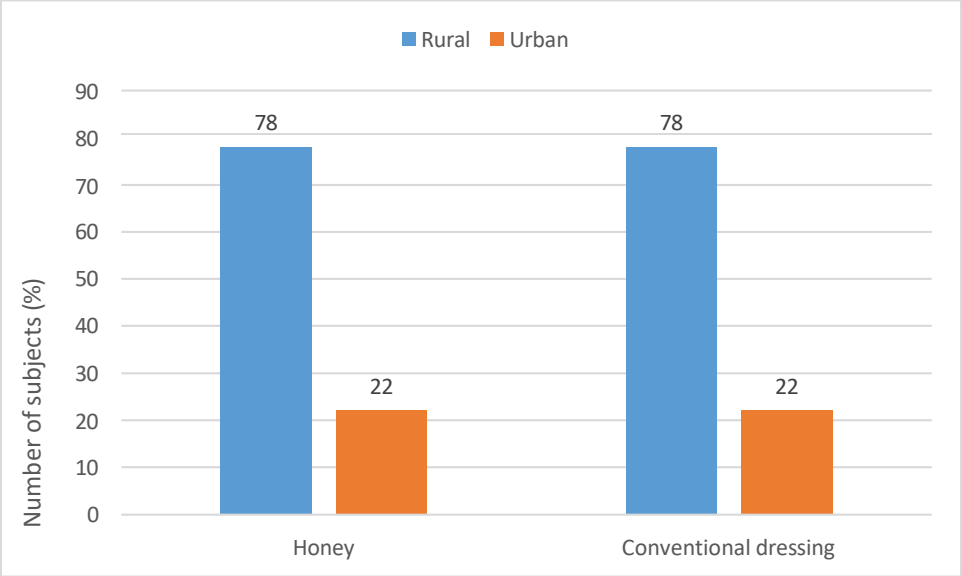


Fig 3: Bar diagram showing Distribution according to place of residence

Table 4: Distribution according to type of wound/ulcer

		Honey		Conventional dressing		Total
		No	%	No	%	
Type of ulcer/wound	Abscess	4	8.0	5	10.0	9
	Burn	11	22.0	11	22.0	22
	Cellulitis	16	32.0	11	22.0	27
	Forniers gangrene	4	8.0	5	10.0	9
	Fungating growth on left malleolus	1	2.0	0	0.0	1
	Multiple boil	0	0.0	1	2.0	1
	No healing ulcer	0	0.0	1	2.0	1
	Post amputation raw area	2	4.0	2	4.0	4
	Post traumatic wound	9	18.0	10	20.0	19
	Pyocele	1	2.0	1	2.0	2
	Stitch granuloma	1	2.0	1	2.0	2
	Tropical ulcer	1	2.0	1	2.0	2
	Venous ulcer	0	0.0	1	2.0	1
Total		50	100.0	50	100.0	100

In the Honey dressing group, majority of the wounds were diagnosed as cellulitis i.e. 32%, followed by 22% as burns, 18% as post traumatic wounds, 8% as abscess and Fournier's gangrene each.

In the conventional dressing group, majority of the wounds were diagnosed as burns and cellulitis i.e.

22% each and 20% as post traumatic wounds.

Fig 4: Bar diagram showing Distribution according to type of wound/ulcer

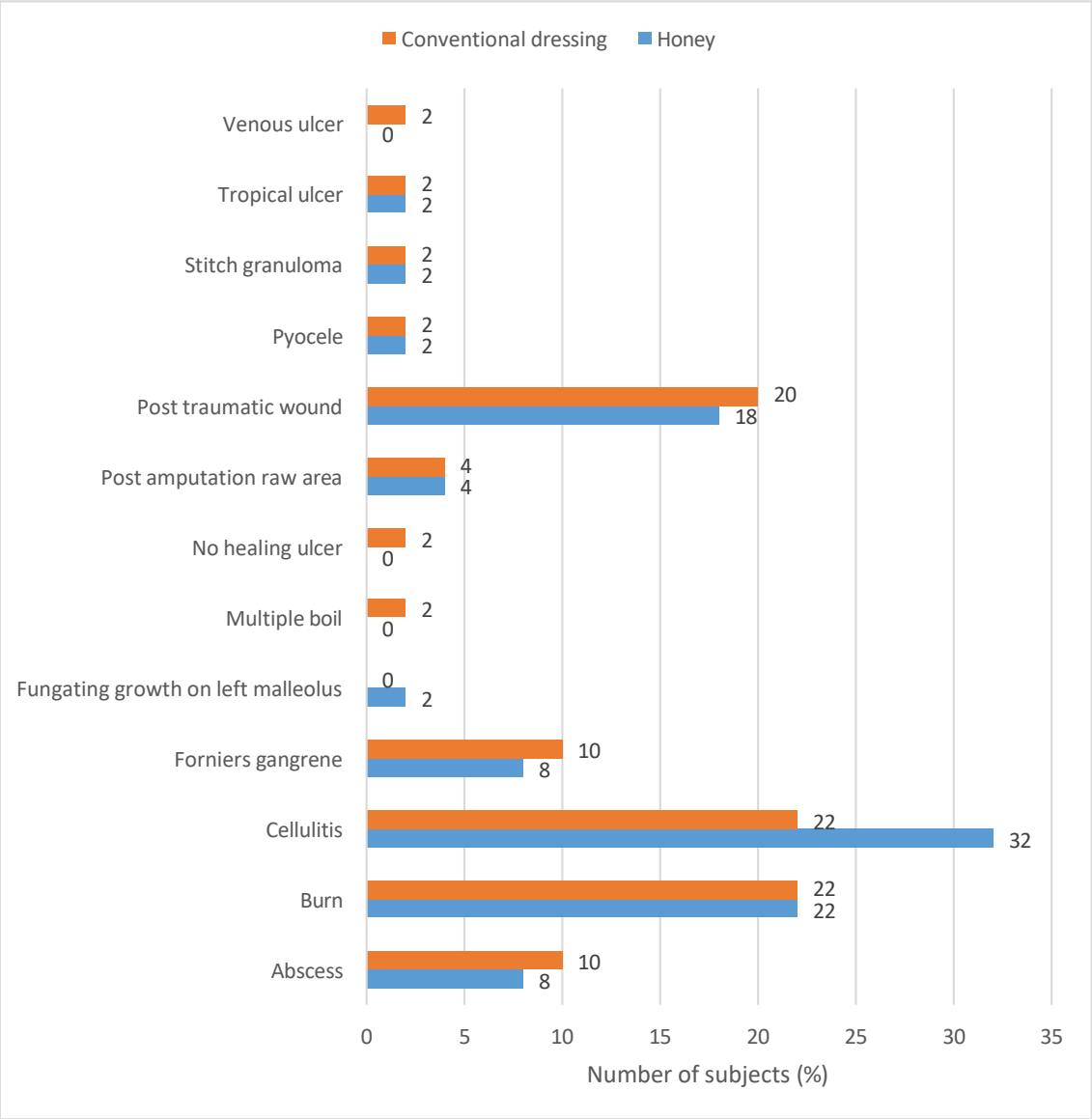


Table 5: Distribution according to risk factors

		Honey		Conventional dressing		Total
		No	%	No	%	
Risk factors	DM	0	0	0	0	0
	HTN	21	42.0	21	42.0	42
	CHD	16	32.0	16	32.0	32
	Smoking	6	12.0	6	12.0	12
	Alcohol	13	26.0	13	26.0	26

We also matched the risk factors in both groups. Accordingly, 42% had hypertension, 32% had CHD, 12% were smokers and 26% were alcoholics in each group.

Fig 5: Bar diagram showing Distribution according to risk factors

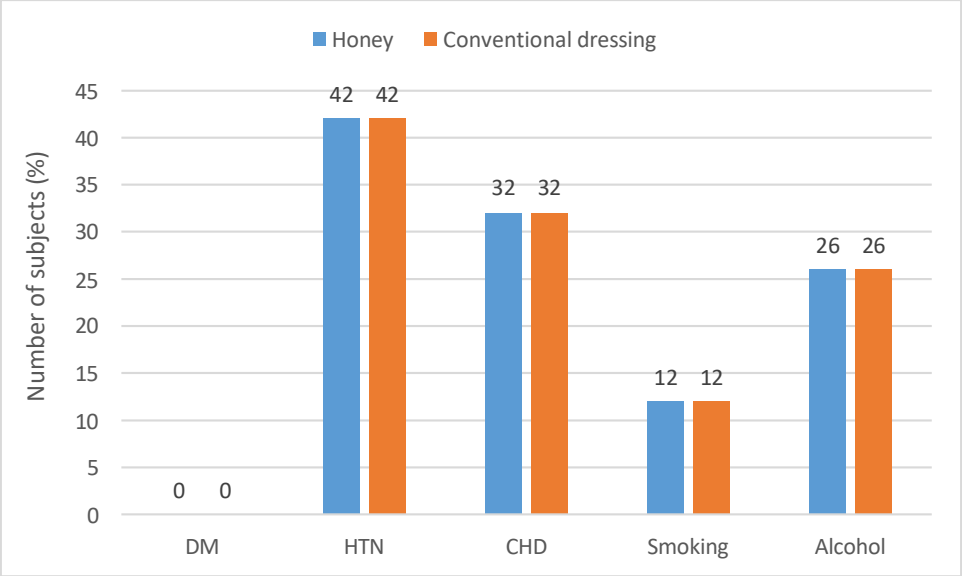


Table 6: Compaison of mean surface area between treatment groups at the start of treatment

Group		N	Mean	Std. Deviation	t	p	Inferenc e
Surface area Before treatmen t	Conventiona l dressing	50	164.66	336.42	1.860	0.590 (>0.05)	Not significan t
	Honey	50	71.44	107.82			

The mean surface area of ulcer before start of treatment in conventional dressing group was 164.66±336.42 cm and in honey dressing group was 71.44±107.82. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically not significant (p>0.05).

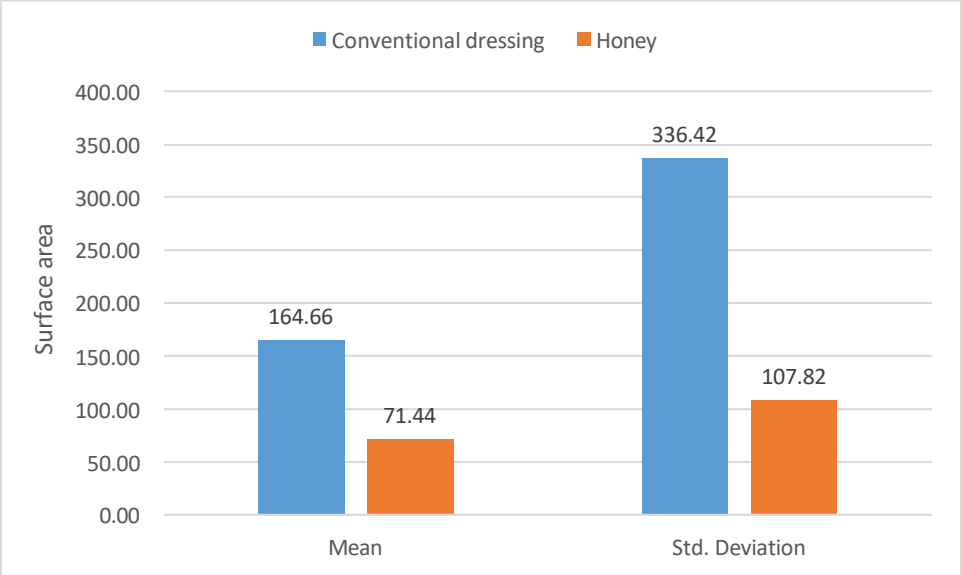


Fig 6: Bar diagram showing Comparison of mean surface area between treatment groups at the start of treatment

Table 7: Comparison of mean surface area between treatment groups at 2 weeks after the start of treatment

Group		N	Mean	Std. Deviation	t	p	Inference
Surface area at WK 2	Conventional dressing	50	103.53	208.73	2.760	0.049 (<0.05)	Significant
	Honey	50	50.27	58.41			

The mean surface area of ulcer at 2 weeks after the start of treatment in conventional dressing group was 103.53±208.73 cm and in honey dressing group was 50.27±58.41cm. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the surface area was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

Fig 7: Bar diagram showing Comparison of mean surface area between treatment groups at 2 weeks after the start of treatment

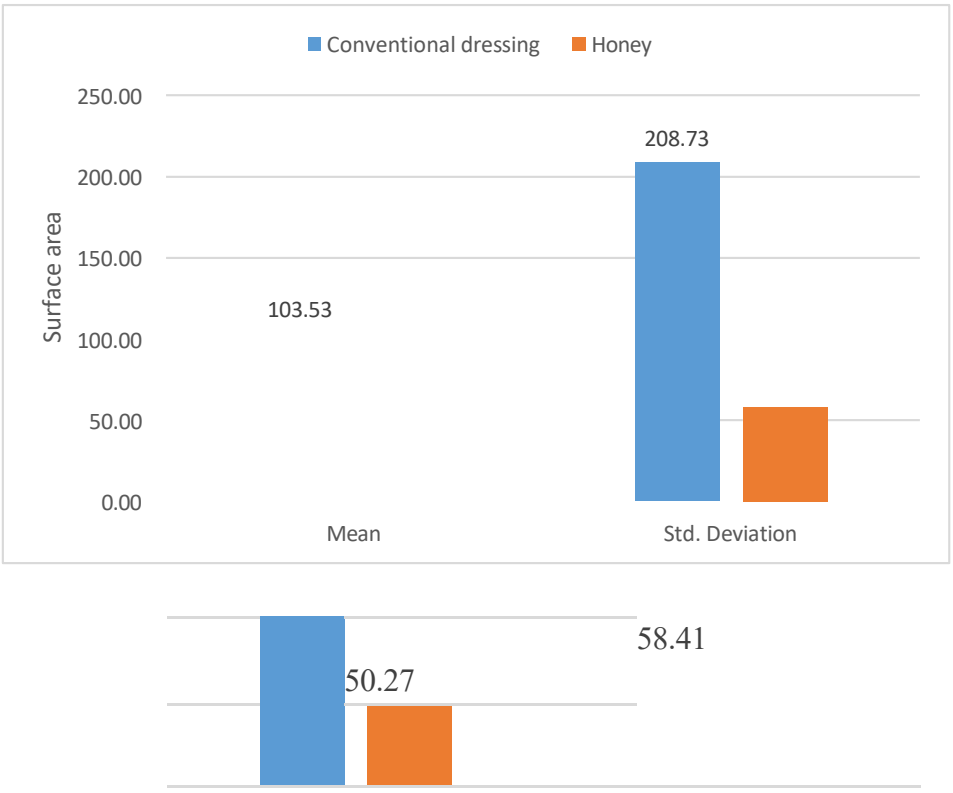


Table 8: Comparison of mean surface area between treatment groups at 4 weeks after the start of treatment

Group		N	Mean	Std. Deviation	t	p	Inference
Surface area at WK 4	Conventional dressing	48	58.95	119.02	2.590	0.040 (<0.05)	Significant
	Honey	46	29.85	35.23			

The mean surface area of ulcer at 4 weeks after the start of treatment in conventional dressing group was 58.95±119.02 cm and in honey dressing group was 29.85±35.23 cm. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the surface area was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

Fig 8: Bar diagram showing Comparison of mean surface area between treatment groups at 4 weeks after the start of treatment

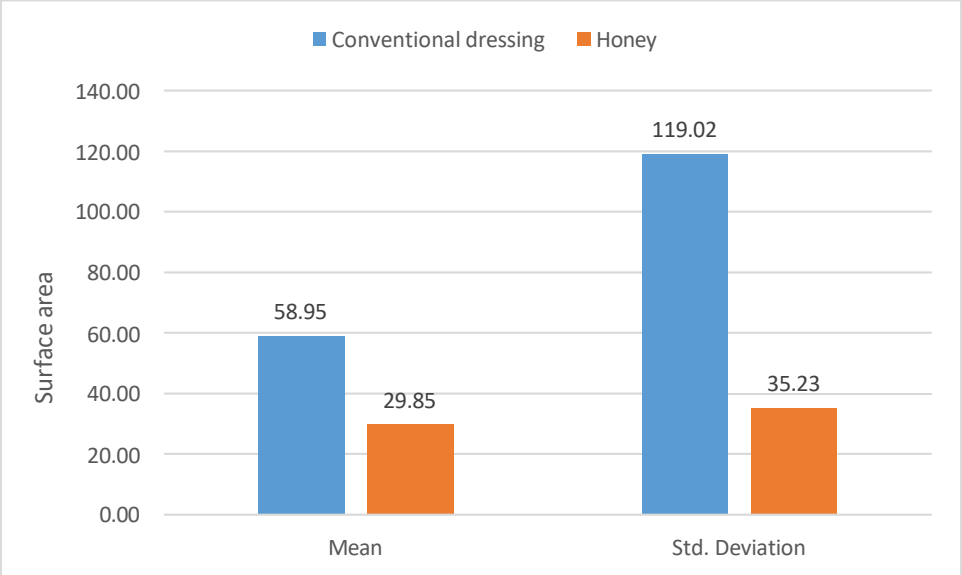


Table 9: Comparison of mean surface area between treatment groups at 6 weeks after the start of treatment

Group		N	Mean	Std. Deviation	t	p	Inference
Surface area at WK 6	Conventional dressing	25	37.17	89.69	2.660	0.036 (<0.05)	Significant
	Honey	21	25.24	31.80			

The mean surface area of ulcer at 6 weeks after the start of treatment in conventional dressing group was 37.17±89.69 cm and in honey dressing group was 25.24±31.80 cm. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically significant ($p<0.05$).

It means the surface area was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

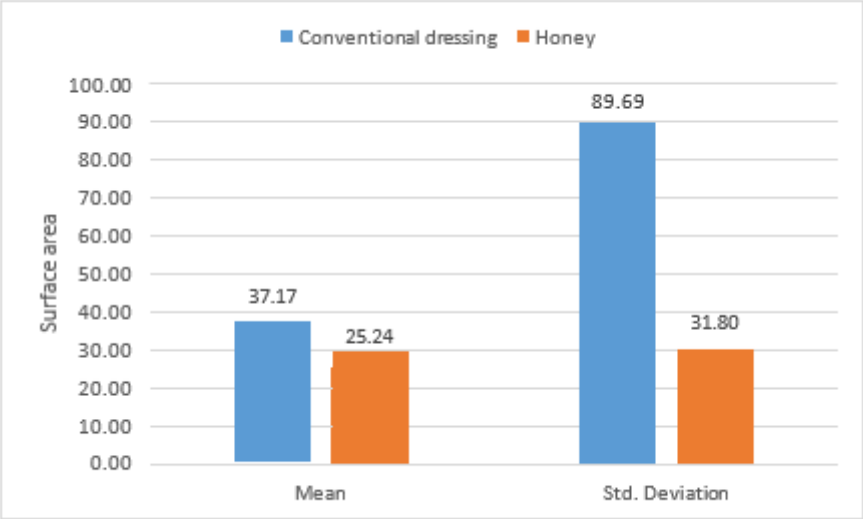


Fig 9: Bar diagram showing Comparison of mean surface area between treatment groups at 6 weeks after the start of treatment

Table 10: Comparison of mean VAS score between treatment groups at the start of treatment

Group		N	Mean	Std. Deviation	t	p	Inference
VAS Before treatment	Conventional dressing	50	7.92	1.23	- 0.087	0.931 (>0.05)	Not significant
	Honey	50	7.94	1.06			

The mean VAS score before start of treatment in conventional dressing group was 7.92±1.23 and in honey dressing group was 7.94±1.06. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically not significant (p>0.05).

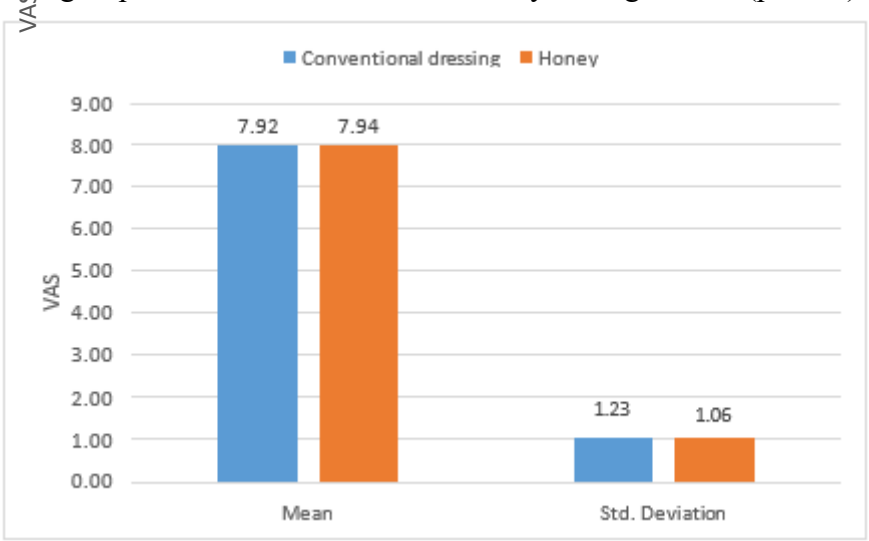


Fig 10: Bar diagram showing Comparison of mean VAS score between treatment groups at the start of treatment

Table 11: Comparison of mean VAS score between treatment groups at 2 weeks after the start of treatment

Group		N	Mean	Std. Deviation	t	p	Inference
VAS at WK 2	Conventional dressing	50	6.16	1.23	2.699	0.008	Highly Significant
	Honey	50	5.56	0.97		(<0.01)	

The mean VAS score at 2 weeks after start of treatment in conventional dressing group was 6.16±1.23 and in honey dressing group was 5.56±0.97. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the VAS score (pain) was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

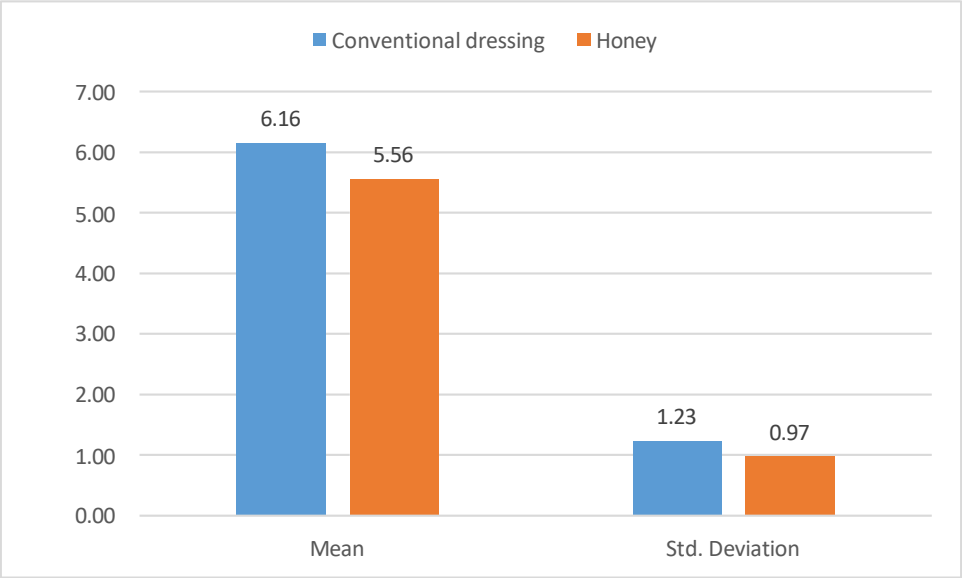


Fig 11: Bar diagram showing Comparison of mean VAS score between treatment groups at 2 weeks after the start of treatment

Table 12: Comparison of mean VAS score between treatment groups at 4 weeks after the start of treatment

Group		N	Mean	Std. Deviation	t	p	Inference
VAS at WK 4	Conventional dressing	48	3.23	0.88	2.330	0.027	Significant
	Honey	42	2.98	0.87		(<0.05)	

The mean VAS score at 4 weeks after start of treatment in conventional dressing group was 3.23±0.88 and in honey dressing group was 2.98±0.87. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the VAS score (pain) was significantly reduced in honey dressing group as compared to conventional dressing

group in our study.

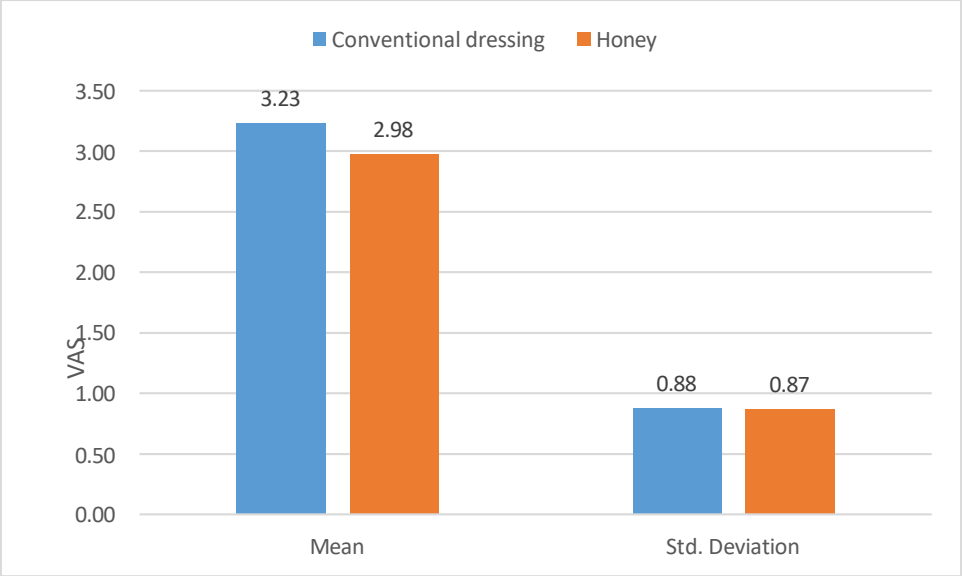


Fig 12: Bar diagram showing Comparison of mean VAS score between treatment groups at 4 weeks after the start of treatment

Table 13: Comparison of mean VAS score between treatment groups at 6 weeks after the start of treatment

Group		N	**Mean**	**Std. Deviation**	**t**	**p**	**Inference**
VAS at WK 6	Conventional dressing	25	3.01	0.71	- 2.625	0.012	Significant
	Honey	21	1.99	0.90		(<0.05)	

The mean VAS score at 6 weeks after start of treatment in conventional dressing group was 3.01±0.71 and in honey dressing group was 1.99±0.90. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the VAS score (pain) was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

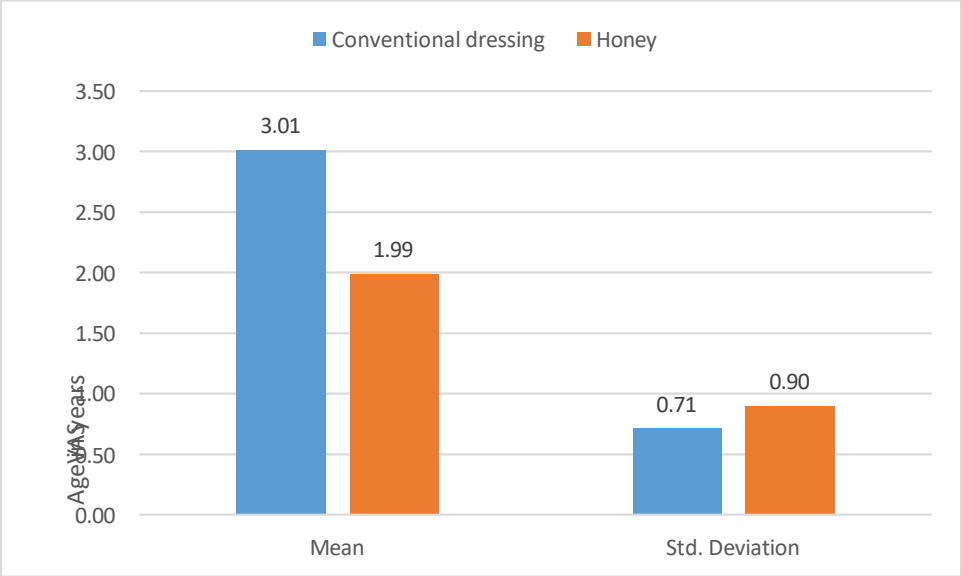


Fig 13: Bar diagram showing Comparison of mean VAS score between treatment groups at 6 weeks after the start of treatment

Table 14: Comparison of mean age group between treatment groups

Group		N	**Mean**	**Std. Deviation**	**t**	**p**	**Inference**
Age	Conventional dressing	50	49.92	20.25	- 0.010	0.990 (>0.05)	Not Significant
	Honey	50	49.96	20.26			

The mean age in conventional dressing group was 49.92±20.25 years and in honey dressing group was 49.96±20.26. When we compared the difference in the mean age between two treatment groups, it was found to be statistically not significant (p>0.05).

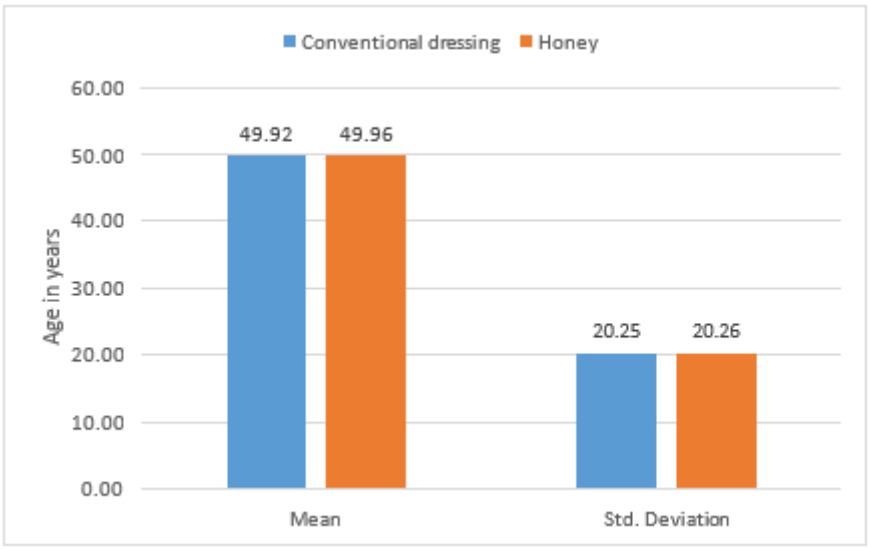


Fig 14: Bar diagram showing Comparison of mean age group between treatment groups

Table 15: Comparative evaluation of appearance of granulation tissue between treatment groups

	Honey		Conventional dressing	
	No	%	No	%
Week 2	31	62.0	15	30.0
Week 4	14	28.0	13	26.0
Week 6	5	10.0	22	44.0

We observed that granulation tissue appeared in 62% cases in honey dressing and 30% cases in conventional dressing at the end of 2nd week, in 28% cases in honey dressing and 26% cases in conventional dressing at the end of 4th week and in 10% cases in honey dressing and 44% cases in conventional dressing at the end of 6th week.

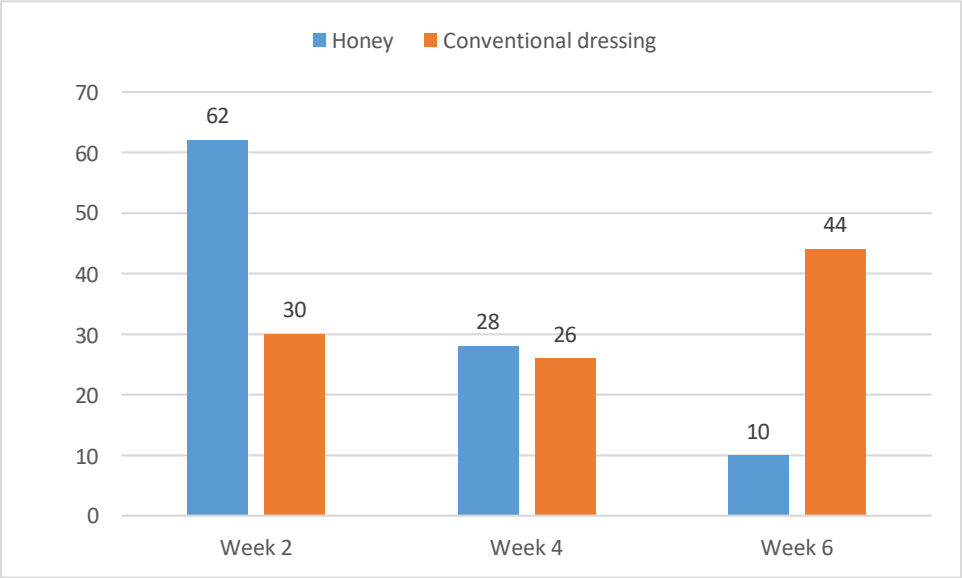


Fig 15: Bar diagram showing Comparative evaluation of appearance of granulation tissue between treatment groups

Discussion

It has been for a long time that honey is using to accelerate the wound healing. It is an excellent adjuvant for acceleration of wound healing, is widely accepted in folk medicine. The exact molecular mechanism of wound healing using honey is yet to be elucidated. Studies showed that it act by reducing ROS levels, besides this it exert antibacterial activity and low pH and high free acid content may assist wound healing. However, several recommendations are made regarding appropriate wound dressing with honey. Type of wound and degree of severity will effect efficacy. Selected honey should be used in sufficient quantities so that it remains there if diluted with wound exudates. It should cover and extend beyond the wound margins. Better results occur when applied on dressing than on wound. All the cavities should be adequately filled with honey and occlusive dressing applied to prevent oozing from the wound. **105**

The effect of honey in wound healing is the result of the combined effects of chemical debridement of dead and devitalized tissues from ulcers by catalase, absorption of edema by the hygroscopic properties of honey, the promotion of granulation and epithelization from wound edges, the bactericidal and

fungicidal properties of honey, its nutritional properties and the production of hydrogen peroxide. Honey comprises 40% glucose, 40% fructose, 20% water, with organic acids, vitamins, enzymes, and minerals; it has specific weight of 1.4 and pH of 3.6. [105]

The treatment with honey is simple and in expensive, and honey need not to be sterile as it already possesses a bactericidal property, because of its high viscosity it forms a physical barrier, creating a moist environment which appears to be helpful and accelerates wound healing1. In observational groups, complete healing was present in this group of patients within two weeks, a good improvement was there in most of the cases, while in case of controlled clinical trials patients reported improvement but the time of improvement varies compare to control groups. [105]

We included total 50 chronic non diabetic non healing wounds in two groups. One groups of wounds was treated with honey and other group was treated with conventional dressing. We matched age groups in both the treatment groups. Majority of the patients

i.e. 22(44%) were from 41-60 years age group in both groups, followed by 15(30%) from 61-80 years, 7(14%) from 21-40 years and least i.e. 6(12%) from 1-20 years age group. We matched gender in both the treatment groups. Accordingly, 62% were males and 38% were females in both the groups.

In the Honey dressing group, majority of the wounds were diagnosed as cellulitis i.e. 32%, followed by 22% as burns, 18% as post traumatic wounds, 8% as abscess and Fournier's gangrene each. In the conventional dressing group, majority of the wounds were diagnosed as burns and cellulitis i.e. 22% each and 20% as post traumatic wounds.

The mean surface area of ulcer at 2 weeks, 4 weeks and 6 weeks after the start of treatment in conventional dressing group was 103.53±208.73 cm and in honey dressing group was 50.27±58.41cm, in conventional dressing group was 58.95±119.02 cm and in honey dressing group was 29.85±35.23 cm., in conventional dressing group was 37.17±89.69 cm and in honey dressing group was 25.24±31.80 cm. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the surface area was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

The mean VAS score at 2 weeks after start of treatment in conventional dressing group was 6.16±1.23 and in honey dressing group was 5.56±0.97. The mean VAS score at 4 weeks after start of treatment in conventional dressing group was 3.23±0.88 and in honey dressing group was 2.98±0.87. The mean VAS score at 6 weeks after start of treatment in conventional dressing group was 3.01±0.71 and in honey dressing group was

1.99±0.90. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the VAS score (pain) was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

Medhi B. et al[105]evaluated the efficacy of topical application honey in observational studies as well as in controlled clinical trials in the treatment of wound healing. A systematic literature search was carried out from 1966 to 31 July 2008 in Pubmed, Medline, Embase, Cochrane database using the appropriate search key words. We found 5 observational studies with 160 patients while 963 cases in 10 controlled clinical trials where 511 patients were treated with honey. Efficacy was found highly efficacious in observational studies but in controlled clinical trial showed its modest efficacy. Most of the patients reported with complete healing of 99% within 2-9 weeks in observational and 56 % in controlled trials and healing was observed within 4-12 weeks' time in controlled clinical trials however some of the recent double-blind trial showed no superior benefit of honey compare to control.

Till date several non-comparative studies have been conducted for the use of honey as a wound dressing, there are no report of cross over trial, though only few double-blind trials have been conducted since it is difficult because of properties of honey, so there is a need for more number of double blind randomized controlled clinical trial. Most of the earlier randomized studies conducted in the past have not given detail of statistical analysis so meta-analysis cannot be plan to make a conclusive remark. Some of the important factors are not taken in to consideration in most of the studies is composition of honey, underlying etiology of wound, nutritional status, age of patients and efficacy of honey in wound healing in different anatomical site of body. So the real efficacy of honey only can be established from more number of double blind RCT with adequate number patients of honey in the treatment of wound healing.[106] **Ingle et al**[107], reported a prospective, randomized, double-blind study comparing the effect of honey and Intrasite gel. The mean healing times of shallow wounds treated with honey or with Intrasite gel did not differ significantly. When adjusted for wound size, the 2.8-day difference in favour of honey was not significant. In the case of abrasions there was also no significant difference. In conclusion of the study, there was no evidence of a real difference between honey and IntraSite gel as healing agents. Another double-blind controlled study with 100 patients was carried out by **McIntosh**[106]**,** revealed that conventional treatment was superior to topical honey application in partial avulsion wounds. Similarly, **Jull et al**[108] also showed modest efficacy 56.6% with honey treatment and most of the patients reported healing in 12 weeks' time.

Summary and Conclusion

Summary

The present prospective experimental interventional hospital based comparative study was carried out at General Surgery OPD and ward at Tertiary Health Centre including 100 patients with clinically diagnosed chronic non healing ulcers and wounds during the study period from October 2019 to october2021 with the objective to study the effect of Honey on Treatment for Chronic Wounds Compared to Standard Therapy.

The results of our study are summarized as follows:

We included total 50 chronic non diabetic non healing wounds in two groups. One groups of wounds was treated with honey and other group was treated with conventional dressing. We matched age groups in both the treatment groups. Majority of the patients i.e. 22(44%) were from 41-60 years age group in both groups, followed by 15(30%) from 61-80 years, 7(14%) from 21- 40 years and least i.e. 6(12%) from 1-20 years age group.

We matched gender in both the treatment groups. Accordingly, 62% were males and 38% were females in both the groups.

78% of patients in both the group were from rural area whereas 22% were from urban area.

In the Honey dressing group, majority of the wounds were diagnosed as cellulitis i.e. 32%, followed by 22% as burns, 18% as post traumatic wounds, 8% as abscess and Fournier's gangrene each.

In the conventional dressing group, majority of the wounds were diagnosed as burns and cellulitis i.e. 22% each and 20% as post traumatic wounds.

We also matched the risk factors in both groups. Accordingly, 42% had hypertension, 32% had CHD, 12% were smokers and 26% were alcoholics in each group.

The mean surface area of ulcer before start of treatment in conventional dressing group was 164.66±336.42 cm and in honey dressing group was 71.44±107.82. When we compared the difference in

the mean surface area between two treatment groups, it was found to be statistically not significant ($p>0.05$).

The mean surface area of ulcer at 2 weeks after the start of treatment in conventional dressing group was 103.53±208.73 cm and in honey dressing group was 50.27±58.41cm. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the surface area was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

The mean surface area of ulcer at 4 weeks after the start of treatment in conventional dressing group was 58.95±119.02 cm and in honey dressing group was 29.85±35.23 cm. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the surface area was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

The mean surface area of ulcer at 6 weeks after the start of treatment in conventional dressing group was 37.17±89.69 cm and in honey dressing group was 25.24±31.80 cm. When we compared the difference in the mean surface area between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the surface area was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

The mean VAS score before start of treatment in conventional dressing group was 7.92±1.23 and in honey dressing group was 7.94±1.06. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically not significant ($p>0.05$).

The mean VAS score at 2 weeks after start of treatment in conventional dressing group was 6.16±1.23 and in honey dressing group was 5.56±0.97. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the VAS score (pain) was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

The mean VAS score at 4 weeks after start of treatment in conventional dressing group was 3.23±0.88 and in honey dressing group was 2.98±0.87. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the VAS score (pain) was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

The mean VAS score at 6 weeks after start of treatment in conventional dressing group was 3.01±0.71 and in honey dressing group was 1.99±0.90. When we compared the difference in the mean VAS score between two treatment groups, it was found to be statistically significant ($p<0.05$). It means the VAS score (pain) was significantly reduced in honey dressing group as compared to conventional dressing group in our study.

The mean age in conventional dressing group was 49.92±20.25 years and in honey dressing group was 49.96±20.26. When we compared the difference in the mean age between two treatment groups, it was found to be statistically not significant ($p>0.05$).

We observed that granulation tissue appeared in 62% cases in honey dressing and 30% cases in conventional dressing at the end of 2^{nd} week, in 28% cases in honey dressing and 26% cases in conventional dressing at the end of 4^{th} week and in 10% cases in honey dressing and 44% cases in conventional dressing at the end of 6^{th} week.

Conclusion

- Honey is effective in reducing wound surface area in our study.
- Honey is also effective in terms of appearance of granulation tissue and reducing pain compared to conventional dressing

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