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# A Randomized Trial of Honey Versus Povidone Iodine Dressings: Pain Profile of Wagner Grade 2 Diabetic Foot Ulcers

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***Authors' contributions***

*This work was carried out in collaboration between both authors. Author CII conceptualized, designed the study, wrote the protocol, and first drafted the manuscript. Author ECI contributed to conceptualization, literature searches, review and edition of the manuscript. Both authors read and approved the final manuscript.*

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## ABSTRACT

Diabetic foot ulcers (DFU), a chronic disorder of public health importance arise from pathologic changes following abnormal glucose metabolism. Wound dressing is vital to DFU management and is designed to promote healing and relieve pain among other roles. Pain associated with chronic wounds can delay healing, reduce quality of life, and affect mental health.
This study evaluates the effect of honey and povidone iodine-based dressings on the severity of pain associated with Wagner grade 2 DFU.
**Study Design:** This was a randomized controlled trial on the pain-modulating effects of honey and povidone iodine dressings on Wagner grade 2 DFU using the visual analogue scale (VAS) at the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt over a year duration.

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**Methodology:** We included 30 patients (17 males; age range 47-65 years) with Wagner grade 2 diabetic foot ulcers. Data on socio-demographics, BMI, HbA1c, ulcer etiology and site distribution, VAS for pain intensity, wound exudate characteristics and extent of healing were obtained and analyzed using Statistical Package for the Social Sciences (SPSS) 20.0. A p-value <0.05 was considered significant**.**
**Results:** The median VAS pain score was 2.0 and 3.0 for the honey and povidone iodine dressing groups respectively (p-value=0.724) in week 1, then 1.0 and 2.0 for the honey and povidone iodine dressing groups respectively and (p-value=0.041) in week 3. By week 5, all ulcers in the honey group were healed, and the lone persistent ulcer in the povidone group had a 1.0 VAS score by week 6.
**Conclusion:** Honey dressings are associated with less wound pain over the course of treatment compared to povidone iodine dressing in the treatment of Wagner 2 DFU.

*Keywords: Diabetic ulcer; dressing; povidone-iodine; honey; wound pain; visual analogue scale; public health.*

## 1. INTRODUCTION

Diabetic foot ulcers (DFU) are a global public health concern that arises from impaired glucose metabolism in diabetes mellitus [1,2] The resulting pathophysiologic changes, primarily angiopathy, neuropathy, and reduced immunity produce limb ulceration, infection, and gangrene [3,4]. Advanced glycation end-products deposited in tissues cause peripheral nerve damage, accelerated atherosclerosis, delayed growth of collateral vessels, and impaired healing [5]. Autonomic dysfunction causes anhydrosis and easy-cracking skins that allow bacterial invasion [6]. Also, impaired bacterial phagocytosis and reduced cell-mediated immunity promote polymicrobial infection [6,7].

DFU result in significant morbidity including ulcer pain, lower quality of life, and eventually cause death if glycemic control remains poor, as observed in nearly 10% of medical deaths [8,9]. Pain from dressing change in DFU is often underestimated, and can lead to depression, anxiety, inactivity, and disturbed sleep, ultimately affecting the overall mental health of patients [10,11]. In Nigeria, the prevalence of DM foot lesions is 0.9- 8.3% and rising [12,13]. Over 15% of diabetics develop DFU in their lifetime, associated with physical, psychological, and economic disability [8,13,14]. DFU account for over 80% of non-traumatic, lower limb amputations with attendant life-altering sequelae, particularly in resource-limited settings [8,15]. Improving the quality of life requires removing the distressing wound symptoms because the emotional component such as sadness, anger, anxiety, emotions of threat, hopelessness, and motivation loss often accompany the sensory painful experience [16].

The study of ulcer and limb pain is generating renewed public health interest [17]. The intricacy of DFU and the features of the corresponding wound-related pain may affect the precision of pain measurement, while underlying comorbidities, such as severe peripheral neuropathy, ischaemia or local inflammation, oedema, foot deformities, or poor foot biomechanics, can make it difficult to diagnose pain [9]. Data from the psychological assessment of persons with chronic pain indicate high rates of psychopathology, amplified by pathologic wound exudate and odor, along with actual and perceived discrimination and social isolation [9,18]. Clinically substantial anxiety or depression was found in 30–35% of inpatients suffering from pain [19]. Hence the growing relevance of pain assessment tools like the visual analogue scale (VAS), verbal rating scale (VRS), and short form-brief pain inventory (SF-BPI).[18] Nevertheless, there is not enough data to suggest the superiority of a single pain evaluation instrument over others for lower limb wounds [9]. Hence, the inclusion of diverse classes of professionals in the hospital and community settings in the care of these persons [8].

The VAS, a psychometric response scale is used to indirectly measure subjective parameters such as pain, indicating a spot along a continuous line between two end-points (0 to 100mm apart) which represent the extremes of the character being assessed. It is often considered the gold standard in pain research [18,20]. About 95.2% of subjects were found to be capable of reading the VAS in concordance with a physician reading, with a precision error of ±2mm [20].

Multidisciplinary management focused on patient education, good glycaemic control, regular foot

examinations and aggressive intervention (debridement, antibiotic therapy, regular dressing) are fundamental to the care of the diabetic foot [13,21]. Good glycaemic control lowers the risk of neuropathy by 40-60% [22].

In addition to providing physical and antimicrobial protection, wound dressings should reduce pain, provide a moist environment, absorb exudates, control odour, and be inexpensive [23,24]. There is yet no perfect dressing for DFU [16]. The wound characteristics i.e. appearance and exudate, guide the choice of dressing [25]. Recent studies, support the use of topical therapies for wound management [26,27].

The therapeutic use of honey spans centuries [28,29]. Honey is a supersaturated sugar solution made by bees, from nectar or other plant fluids [30,31]. It contains 80–85% carbohydrates (mostly glucose and fructose), 15–17% water, 0.1–0.4% protein, 0.2% ash, amino acids, vitamins, and phenolic antioxidants [32]. Its hydrogen peroxide, inhibin, and high acidity(pH 3.2-4.2) inhibit bacterial proliferation [33,34]. It reduces inflammation, debrides necrotic tissues, enhances granulation tissue, deodorizes infected wounds, reduces pain, promotes epithelization, and minimizes scarring when used topically [33,35]. Its soothing effect is attributed largely to its capacity to conserve moisture, prevent adherence to wound beds, and preserve nascent granulation tissue and keratinocytes during the change of dressing [28,33].

Povidone-iodine is a loose mixture of iodine and a non-ionic surfactant [26,36]. Its antimicrobial activity is maximal after dilution due to the weakened link between the carrier polymer and iodine molecules, leading to the increased amount of elemental 'free' iodine released into solution until an equilibrium is reached, after which the povidone iodine reservoir releases additional 'free' iodine while the iodine-consuming germicidal action continues [26,36,37]. This inhibits inflammation caused by infections and the host response thereby indirectly reducing pain [26]. Despite its widespread use, acquired resistance to it remains rare [26,37].

Several DFU classification systems exist [6,38]. However, the Wagner classification which considers the ulcer depth, presence of osteomyelitis, and amount of tissue gangrene, is most widely utilized. [6,38] Wagner Grade 2 ulcers are deep ulcers to the tendon, bone, ligament, or joint involvement [38].

By evaluating the effect of honey and povidone iodine dressing on DFU pain, this study seeks to support the quest for cheaper, effective, and readily available wound dressing materials that are invaluable globally, particularly in low-resource settings, where access to affordable, high-quality healthcare is challenging.

## 2. METHODOLOGY

### 2.1 Study Design

This was a randomized controlled trial comparing ulcer pain following honey and povidone iodine dressing among patients with Wagner grade 2 DFU who presented to the UPTH via the orthopedic clinic and medical wards between April 1st 2017 and April 30th, 2018.

### 2.2 Sample Size Determination

Sample size was calculated using $n = \frac{2\,(Z\alpha+Z\beta)^2 s^2}{d^2}$ , being the formula for comparison of groups [39]; where *'n'* is the minimum sample size, '*Zα'* is the significance level of 95% (with a value of 1.96), '*Zβ'* represents the power of 80 (corresponding to 0.84), '*S'* signifies standard deviation(SD) - the SD of the rate of healing of DFU using honey dressing from a similar study was 0.94 [40]*, while 'd'* is the level of precision (corresponding to 0.5).

$$\text{Therefore, } n = \frac{2\,(1.96 + 0.84)^2\,(0.94)^2}{(0.5)^2} = \frac{2\,(7.84)\,(0.884)}{0.025} = 55.41$$

To allow for an attrition rate of about 10%, the sample size was rounded up to **60** and adjusted for population <10,000 using the finite population correction (adjusted sample size) formula [39] where **'$n_0$'** (minimum sample size) was 60, and **'N'** (Total population of DFU in UPTH, 2016) was 47.

$$\text{Therefore, the adjusted sample size} = \frac{n_0 N}{n_0 + (N-1)} = \frac{60 \times 47}{60 + (47-1)} = 26.6 \text{ approximated to } 30$$

Hence, a total sample size of 30 comprising of 15 patients per group were involved in the study.

### 2.3 Eligibility Criteria

The subjects were diabetics aged between 30-65 years (lower risk of co-morbidities) with Wagner Grade 2 foot ulcers.

#### 2.3.1 Inclusion criteria

They also met the following criteria:

a. Ankle-brachial pressure index (ABPI) >0.9,
b. Oxygen saturation of ≥92% by pulse oximetry
c. Serum albumin concentration >35g/dl.

#### 2.3.2 Exclusion criteria

The following subjects were excluded from the study.

a. Patients with multiple co-morbidities, severe immunosuppression, malignant disease or chemotherapy, haemoglobinopathies, steroid therapy, and neutrophil count below 2000/mm$^3$.

### 2.4 Study Procedure

#### 2.4.1 Randomization

All subjects who consented to the study and met the inclusion criteria were randomized into two groups; Group A (honey group) and Group B (povidone iodine group) using an opaque envelope containing papers labelled either A or B. A paper was randomly drawn from the envelop for each eligible subject, who was assigned to the group label on the paper.

#### 2.4.2 Blinding

The author was blinded to the dressing for both groups to avoid bias. He was absent at the removal of old dressings, returned to assess the study parameters, and left prior to the new dressings by trained nurses.

#### 2.4.3 Details of the study

Written informed consent was obtained from each patient. Honey obtained from a single commercial local source to ensure uniformity while povidone iodine solution 10% was used in the control dressing group. All subjects received appropriate antibiotics and had surgical debridement by the researcher or trained orthopedic residents. Data on patients' age, gender, body mass index, HbA1c levels, ulcer etiology and ulcer site distribution, were obtained. Glycemic control was maintained by a supervising physician.
Wound dressing was commenced immediately, and performed daily by trained nurses. The wound was first cleansed with normal saline, and dressed with honey or povidone iodine soaked gauze, supported by layers of dry sterile gauze, and then bandaged.

A weekly wound assessment noting the pain VAS score, wound exudate characteristics and extent of healing was performed prior to the change of dressing to avoid bias from the discomfort of the change of dressing. The assessment ended 6 weeks after the initial surgical debridement or when the wound had healed, whichever came earlier.

The consumables used include natural honey, 10% povidone iodine (Betadine®), normal saline, sterile cotton swabs, sterile gauze, crepe bandages, sterile gloves and VAS instrument.

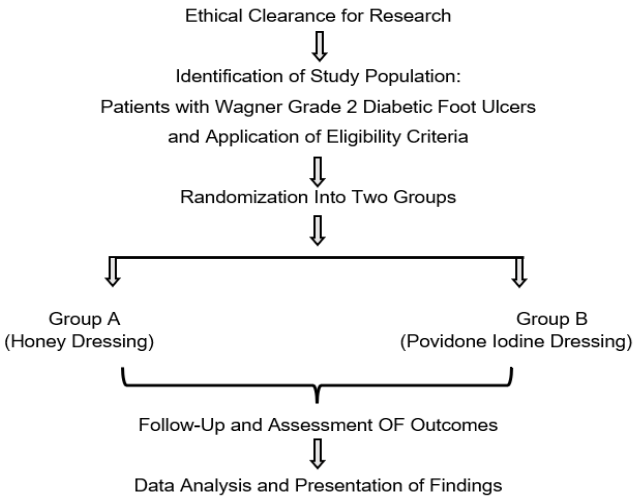


**Fig. 1. Diagrammatic presentation of study protocol**

## 2.5 Data Analysis

Data analysis used the IBM ® Statistical Package for the Social Sciences (SPSS) version 20 and presented as tables and charts. Qualitative variables were stated as frequencies and proportions while quantitative variables such as HbA1c were summarized as means ± standard deviation. Medians and ranges were used to summarize the VAS pain scores. The data were tested for normality by Kolmogorov-Smirnov test prior to analysis. For data with normal distribution (e.g. HbA1c), the differences in means between the groups were compared using the student's t-test, while the Mann-Whitney U test was used to compare differences across the VAS pain score. Chi square test or Fisher's exact test was used to compare the differences in proportions between the groups. A p value < 0.05 was considered statistically significant.

## 3. RESULTS

There were 17 males and 13 females (ratio 1.3:1). The honey group had 7 (46.7%) females, while the povidone iodine group had 9 (60.0%) males. The subjects were aged 47 to 65 years with a mean 55.53±5.041 years for group A, and 54.93±5.298 years in group B(t=0.318; p-value=0.753). The 55-59 years age group (40%) had the highest frequency. The difference in the age (p-value=0.266) and sex (p-value=0.713) distribution was not significant (Table 1).

Most study participants were overweight (63.3%). The difference in proportions of BMI category between both groups was not statistically significant (p-value=0.762). The mean BMI were 27.34±2.783 kg/m2 and 27.99±2.336 kg/m2 in the honey and povidone dressing groups respectively (p-value=0.492) as shown in Table 2.

The median visual analogue scale pain score was 2.0 and 3.0 for the honey and povidone iodine dressing groups respectively (p-value=0.724) in week 1. By week 3, the difference in the median score between the patients in the honey group (1.0) and povidone iodine group (2.0) was statistically significant (p-value=0.041) as shown in Table 3.

Fig. 2 shows the mean pain scores in honey and povidone iodine groups across the follow-up period. Other than Week 1, the pain scores were lower in the honey group in comparison to the povidone iodine group.

**Table 1. Demographic characteristics of the study groups**

| | **Groups in the study** | | |
|---|---|---|---|
| **Variables** | **Honey N=15 n (%)** | **Povidone Iodine N=15 n (%)** | **Total N=30 n (%)** |
| **Age category** | | | |
| 45-49 years | 4 (26.7) | 3 (20.0) | 7 (23.3) |
| 50-54 years | 0 (0.0) | 4 (26.7) | 4 (13.3) |
| 55-59 years | 7 (46.7) | 5 (33.3) | 12 (40.0) |
| >60 years | 4 (26.7) | 3 (20.0) | 7 (23.3) |
| | ***Fisher's exact test=4.432;p-value=0.266*** | | |
| **Sex** | | | |
| Female | 7 (46.7) | 6 (40.0) | 13 (43.3) |
| Male | 8 (53.3) | 9 (60.0) | 17 (56.7) |
| | ***Chi-square=0.136;p-value=0.713*** | | |

**Table 2. BMI status of the study participants**

| | **Groups in the study** | | |
|---|---|---|---|
| **BMI status** | **Honey n (%)** | **Povidone Iodine n (%)** | **Total n (%)** |
| Normal | 3 (20.0) | 2 (13.3) | 5 (16.7) |
| Overweight | 10 (66.7) | 9 (60.0) | 19 (63.3) |
| Obese | 2 (13.3) | 4 (26.7) | 6 (20.0) |
| Total | 15 (100.0) | 15 (100.0) | 30 (100.0) |

*Fisher's exact test=0.983; p-value=0.762*

**Table 3. Comparison of median pain scores (Visual Analogue Scale) across the study groups**

| | Groups in the Study | | | |
|---|---|---|---|---|
| **Time of follow-up** | **Honey Median VAS (Range)** | **Povidone Iodine Median VAS (Range)** | **Mann-Whitney U** | **p-value** |
| Week one | 2.0 (1-4) | 3.0 (1-4) | 104.50 | 0.724 |
| Week two | 2.0 (1-3) | 2.0 (1-3) | 103.00 | 0.663 |
| Week three | 1.0 (1-3) | 2.0 (1-3) | 68.50 | 0.041* |
| Week four | 1.0 (1-1) | 1.0 (1-2) | 8.00 | 0.221 |
| Week five | - | 2.0 (2-2) | - | - |
| Week six | - | 1.0 (1-1) | - | - |

**Statistically significant*

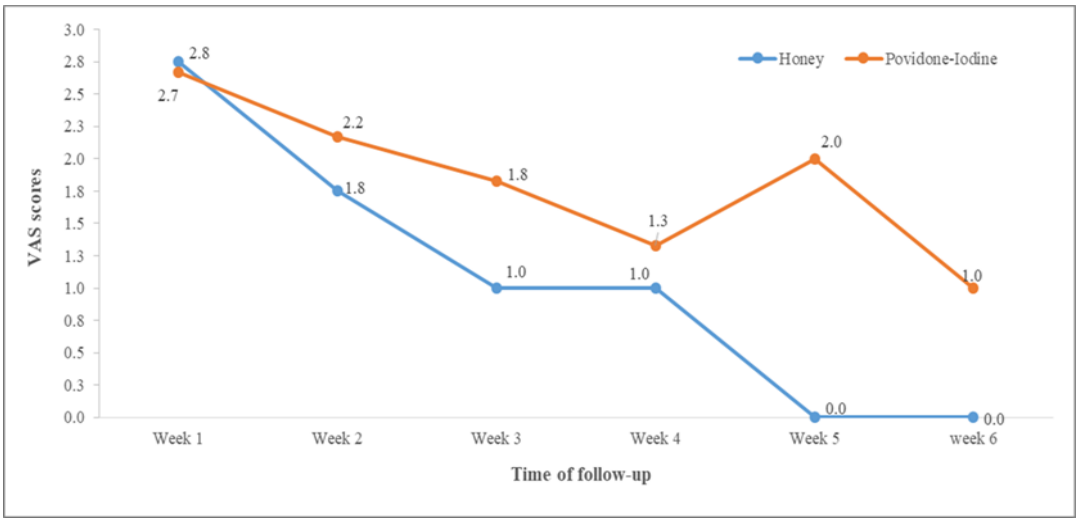


**Fig. 2. Comparison of the mean VAS scores across the follow-up period**

Erectile dysfunction was the commonest DM complication encountered in the povidone iodine group (53.3%), while visual impairment was the most frequent in the honey group (53.3%). One patient had a prior history of a foot ulcer in each study group (6.7%).

In the honey group, 46.7% of the ulcers resulted from trauma, 46.7% developed spontaneously, and 6.7% had burn injury, while ulcers in the povidone iodine group were caused by trauma (33.3%), tight shoes (13.3%) or developed spontaneously (53.4%). The distribution of ulcer causation between the study groups had no significant statistical difference (p-value=0.536) as shown in Table 4.

Left feet were affected by 63.3% of ulcers, while right foot involvement was seen in 36.7% of the study population. The most common site was the dorsum of the left foot (40.0%) as seen in 33% and 46.7% of the honey and povidone groups respectively. The medial aspect of the forefoot and left big toe were the least affected regions (3.3% each). There was no significant difference (p-value=0.392) in the anatomical location between the study groups (Table 5).

**Table 4. Distribution of ulcer etiology**

| | Groups in the study | | |
|---|---|---|---|
| **Ulcer etiology** | **Honey n (%)** | **Povidone-Iodine n (%)** | **Total n (%)** |
| Burn | 1 (6.7) | 0 (0.0) | 1 (3.3) |
| Trauma | 7 (46.7) | 5 (33.3) | 12 (40.0) |
| Tight shoe | 0 (0.0) | 2 (13.3) | 2 (6.7) |
| Spontaneous | 7 (46.7) | 8 (53.4) | 15 (50.0) |
| Total | 15 (100.0) | 15 (100.0) | 30 (100.0) |

*Fisher's exact test=2.992; p-value=0.536*

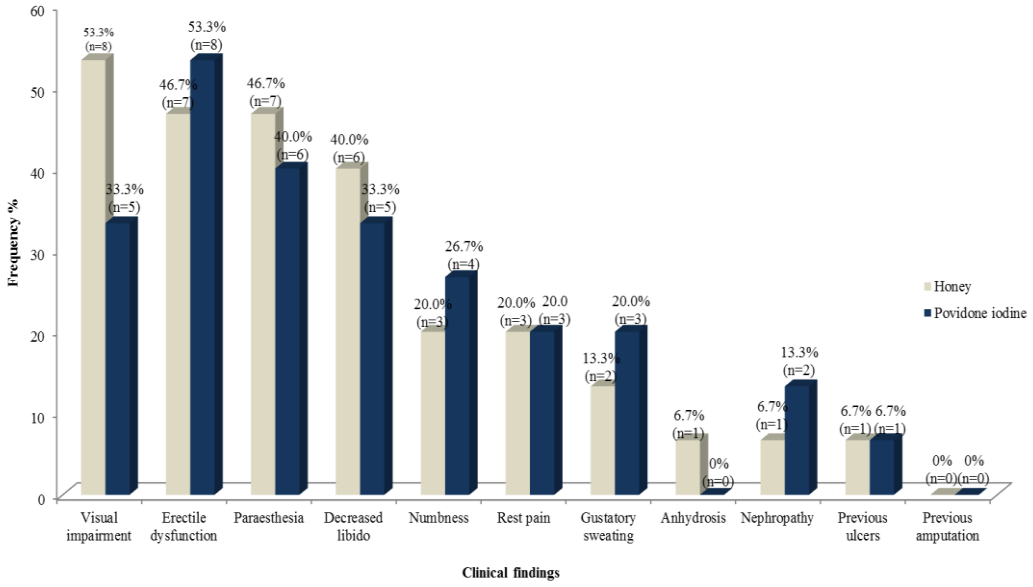


**Fig. 3. Distribution of complications of diabetes mellitus**

**Table 5. Distribution of ulcer sites**

| | Groups in the study | | |
|---|---|---|---|
| **Ulcer site** | **Honey n (%)** | **Povidone-Iodine n (%)** | **Total n (%)** |
| Left big toe | 1 (6.7) | 0 (0.0) | 1 (3.3) |
| Left dorsum | 5 (33.3) | 7 (46.7) | 12 (40.0) |
| Left heel | 2 (13.3) | 0 (0.0) | 2 (6.7) |
| Left sole | 1 (6.7) | 2 (13.3) | 3 (10.0) |
| Left medial forefoot | 0 (0.0) | 1 (6.7) | 1 (3.3) |
| Right Dorsum | 1 (6.7) | 2 (13.3) | 3 (10.0) |
| Right heel | 3 (20.0) | 0 (0.0) | 3 (10.0) |
| Right sole | 2 (13.3) | 3 (20.0) | 5 (16.7) |
| Total | 15 (100.0) | 15 (100.0) | 30 (100.0) |

*Fisher's exact test=7.527; p-value=0.392*

The duration between the development of foot ulcers and the initial debridement ranged from 5-15 days, giving mean values of 8.53±4.533 days and 7.73±2.374 days for the honey and povidone iodine groups respectively. This difference was not statistically significant (p-value=0.550) as shown in Table 6.

The subjects' HbA1c values ranged from 6.3% - 10.2% (mean: 7.40±0.944%) in the povidone iodine group, and 6.7%-9.9% (mean: 7.52±1.023%) for the honey group. This difference in was not significant (p-value=0.727) as seen in Table 6.

None of the respondents in both groups achieved complete wound healing in the first three weeks of follow-up. By week 4, 11(73.3%) and 6 (60.0%) had complete wound healing in honey and povidone iodine groups respectively. By week 5, all patients in honey group had complete wound healing while all but one of the patients in the povidone-iodine group had complete wound healing. The remaining lone DFU persisted till the end of the study period in week 6 as shown in Fig. 4.

In the first week, serosanguinous exudates were seen in 66.7% and 60% of ulcers in the honey and povidone iodine groups respectively, while 6.7% of ulcers in each group had seropurulent exudates. The ulcers with serous exudates made up 26.7% and 33.3% of the honey and povidone iodine groups. By week 2, the ulcers

with serous exudates increased to 66.7% and 73.3% in the honey and povidone iodine groups respectively. However, all exudates turned serous by the third week and remained so until the ulcers were healed or till the end of the study (Table 7).

**Table 6. Comparison of mean duration of ulcers prior to debridement, and mean HbA1c**

| | Groups in the Study | | | |
|---|---|---|---|---|
| **Variables** | **Honey Mean ± SD** | **Povidone Iodine Mean ± SD** | **t** | **p-value** |
| Duration of ulcers (days) | 8.53±4.533 | 7.73±2.374 | 0.605 | 0.550 |
| HbA1c level (%) | 7.52±1.023 | 7.40±0.944 | 0.352 | 0.727 |

*SD – Standard Deviation*

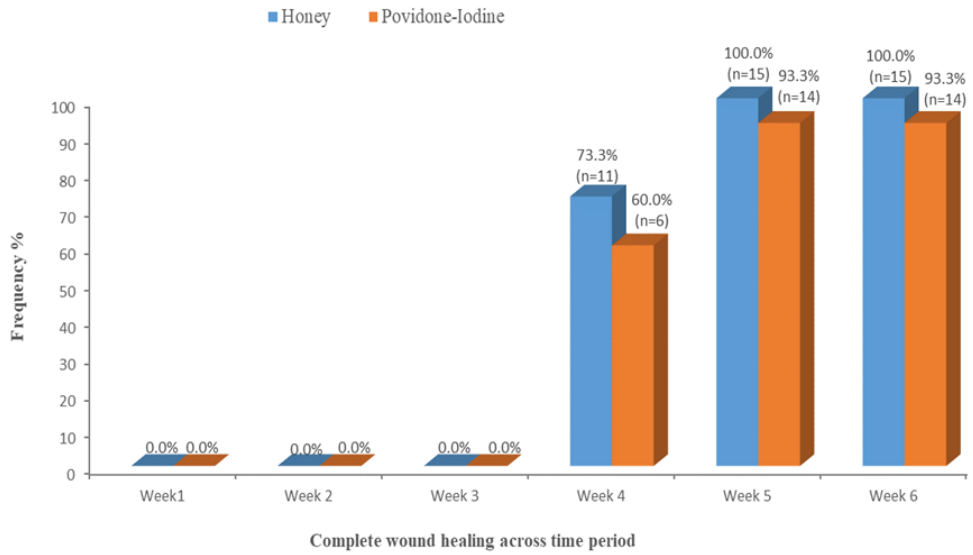


**Fig. 4. Distribution of wound healing across the time period**

**Table 7. Comparison of wound exudate findings across the study period**

| | Groups in the study | | |
|---|---|---|---|
| **Type of exudate** | **Honey (N=15) n (%)** | **Povidone iodine (N=15) n (%)** | **Total n (%)** |
| **Week 1** | | | |
| Seropurulent | 1 (6.7) | 1 (6.7) | 2 (6.7) |
| Serosanguinous | 10 (66.7) | 9 (60.0) | 19 (63.3) |
| Serous | 4 (26.7) | 5 (33.3) | 9 (30.0) |
| **Week 2** | | | |
| Serosanguinous | 5 (33.3) | 4 (26.7) | 9 (30.0) |
| Serous | 10 (66.7) | 11 (73.3) | 21 (70.0) |
| **Week 3** | | | |
| Serous | 15 (100.0) | 15 (100.0) | 30 (100.0) |
| **Week 4** | | | |
| Serous | 4 (26.7) | 6 (40.0) | 10 (33.3) |
| **Week 5** | | | |
| Serous | 0 (0.0) | 1 (6.7) | 1 (3.3) |
| **Week 6** | | | |
| Serous | 0 (0.0) | 1 (6.7) | 1 (3.3) |

## 4. DISCUSSION

The burden of DM and its complications, especially DFU is emphasized by the difficulty faced while seeking patients who met the inclusion criteria, patients expected to be as healthy as possible, since most diabetics already have complications at the onset of foot ulceration [41,42].

This study found that data on demographics, BMI, HbA1c level, and ulcer aetiology, location, and ulcer duration prior to presentation, of both the honey and povidone iodine groups were comparable. The similarity in mean HbA1c between both study groups (p-value=0.727) eliminates HbA1c level as a possible confounding factor especially in relation to neuropathy [43].

Diabetic wounds were once thought to be typically painless. However, it is now known that wound-related pain can occur concurrently irrespective of whether the wound is neuropathic or neuro-ischaemic, as shown in up to 75% of people with DFU and concomitant peripheral neuropathy [9]. The median visual analogue scale pain score was 2.0 and 3.0 for the honey and povidone iodine dressing groups respectively (p-value=0.724) in week 1, then 1.0 and 2.0 for the honey and povidone iodine dressing groups respectively (p-value=0.041) in week 3. This was statistically significant. This is somewhat similar to the findings of Dickinson *et al.* [18] who examined the characteristics of pain associated with DFU and reported an overall median VAS score of 2.0. Mohamed *et al*. [44] and Gulati *et al.*, [45] similarly noted significantly reduced VAS pain scores among patients treated with honey dressings in diverse categories of ulcers compared to povidone iodine, even as Hubalova et al reported that 72% of their subjects experienced a satisfactory reduction in reported levels of wound and dressing pain, thus obviating the need for analgesia [16]. However, in contrast with the study by Dickinson *et al*, no patient in the index study reported 'non-existent' pain [18]. This was probably because their study primarily involved patients with neuropathic and other wound aetiologies who might have had anaesthetic feet/ulcers. Moreover, even in cases of severe neuropathy, wound pain may indicate the onset of limb-threatening complications such deep infection or acute ischaemia, which could impede wound healing [9].

Interestingly, patients have been noted to be unwilling to report pain due to the notion that wound pain is inevitable and must be endured [9]. Others fear a referral for amputation if they accurately report their pain prompting them to deny or devalue it. Therefore, the accuracy of wound pain evaluation and management can be influenced by the level of trust and rapport that exists between patients and healthcare providers [9]. This was not considered during this study [46].

Erectile dysfunction occurred in 88% of the male subjects. However, other causes of erectile dysfunction such as anxiety and drugs such as beta-blockers [43] were not ruled out. Visual impairment, paraesthesia and decreased libido were also reported. In a Tanzanian study, [43] 10.3% of subjects had previous DFU, while Unachukwu *et al.* [47] reported a 33% history of previous ulcers among patients with all grades of DFU. More divergently, Ngwogu *et al*., noted a 10.6%, and 9.2% incidence of peripheral neuropathy and DFU respectively in their study [48].

While 50% of the index ulcers developed spontaneously; trauma, tight shoes and burn injury constituted 40%, 6.7% and 3.3% respectively. Similarly, Unachukwu *et al* [47] observed a 51.7% incidence of spontaneously occurring ulcers. Khan *et al* in Pakistan reported accidental/foot wear-trauma (36%) and foot deformity (46%) [40]. Some of these spontaneous DFU could have resulted from unnoticed (delayed by underlying neuropathy and retinopathy) micro-trauma which became infected [47,48,35].

The dorsum of the left foot (40%) was the most common ulcer site in this study in consonance with the observation of Unachukwu *et al*. [47] The reason for this is unclear. Studies show that 70-90% of the world's population are right hand/foot dominant. [47]. The non-dominant limb may be relatively less perceptive to micro-trauma which goes unnoticed, leading to ulceration, given the background immunosuppression of DM [35,47]. More research is needed on this finding.

The mean duration between the onset of ulcers and the debridement were 8.53±4.533 days and 7.73±2.374 days for the honey and povidone iodine groups respectively. This relatively early presentation suggests good health seeking behaviour which could have been prompted by the health education received at the endocrinology clinic. This may explain the

adequacy of their vascular statuses which enabled them to meet the study's inclusion criteria. Also, ignorance and socio-cultural influences may contribute to late presentation [49]. Ogbera *et al*. noted that 78% of their study respondents believed that 'poisoning' and 'curses' were responsible for foot ulcers [49]. People with such perceptions are inclined to seek spiritual help before presenting to the hospital [50].

The mean healing time of 4.00±0.00 weeks was observed in ulcers in the honey group. Correspondingly, ulcers in the povidone iodine group were healed around 5.00±0.00 weeks. There was no significant difference in the wound healing between the study groups, thus eliminating the rate of healing and physiologic status of the wounds as confounders in the assessment of ulcer pain.

Initially, 63% of exudates were serosanguinous following debridement. Subsequently, all ulcers in both groups had serous exudates by the third week signifying improved healing. Good exudate is typically serous (clear, pale amber, watery and odourless) [51]. Wound exudate have been classified based on quantity as absent (0), small (1), moderate (2), or large (3) [52]. This study opted for qualitative assessment because the clinical appearance has more bearing on the presence or otherwise of infection which can worsen pain, while the mere amount of exudate may correlate more with factors that increase capillary leakage such as limb dependency [52].

The strength of this study is hinged on its design as an RCT to provide substantial evidence on the effect of honey versus povidone iodine on the pain profile of diabetic patients. However, being a single-centre study, this could limit the generalizability of the study, therefore multi-centre studies are recommended.

## 5. CONCLUSION

Complications occur commonly among diabetic patients, with DFU often developing without obvious causes. Honey dressings are associated with less wound pain over the course of treatment thereby better easing patient discomfort and improving their quality of life compared to povidone iodine dressings. It is also important to monitor the nature of exudates produced, as they may serve as pointers to ongoing events in the ulcers.

## CONSENT AND ETHICAL APPROVAL

Ethical approval was obtained from the research and ethics committee of the UPTH prior to the commencement of the study. Written informed consent was obtained from all study participants after being adequately informed about the nature, extent and purpose of the research. Anonymity and confidentiality were upheld in the study. Participation in the study was voluntary, and patients' withdrawal from the study did not affect their medical care.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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