International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 10-08-2020; Accepted: 25-08-2020; Published: 11-09-2020
www.medicalsciencejournal.com
Volume 6; Issue 9; 2020; Page No. 58-64

Don't let diabetes pull down our foot

JA Jayalal MS[1], Karthiyayini[2], Sathik[3]
[1] Professor of Surgery TVMCH, National senior vice president IMA, Tamil Nadu, India
[2] Assistant Professors, Surgery TVMCH, Tamil Nadu, India

Abstract
Diabetic foot is defined as the sore that develops in the foot that develops due to microvascular and macrovascular complications including failure of wound healing process and is the most common problem of diabetes mellitus. The risk factors for development of diabetic foot are Diabetic Neuropathy, Peripheral Vascular Disease, Cigarette smoking, Poor glycemic control, Previous ulceration and Previous Amputation.
The altered metabolism of glucose results in abnormal formation of granulation tissue thereby delays wound healing. Secondly, Nitric oxide is an important stimulator of cell proliferation, maturation and differentiation which also increases fibroblast proliferation and thereby collagen production in wound healing. Hence, impaired nitric oxide synthesis will delay wound healing process. Fibroblasts from diabetic ulcer exhibit proliferative impairment that perhaps contributes to a decreased production of extracellular matrix proteins that delay wound contraction and impaired wound healing.
Diabetic foot problems are wider and several systems including vascular, nervous, somatosensory and musculoskeletal systems have been involved. The biomechanics happens due to effects on skin, tendons and ligaments, effects on cartilages, effects on muscles, effects on peripheral sensory system, and effects on foot morphology.
Diabetes Foot Assessment includes *Complete History,* Duration of illness and treatment received, Glycemic control, Diabetes complications, if any, History of heart disease, History of wound formation and treatment type, Wound healing process, History of amputation and surgery, History of Smoking, Life style habits, exercise pattern, Neuropathic symptoms, if any, Vascular symptoms, if any.
Management principles include Wound Dressing, Infection Control practice, Antibiotics, Offloading, Rest, Elevation of affected foot, Relief of pressure Ultrasonic debridement, Topical growth factors, honey dressing, phenytoin dressing, platelet rich plasma therapy, Bioengineered skin grafts(BATs),VAC (Vacuum Assisted Closure) Therapy, Hyperbaric oxygen therapy(HBOT), Stem cell therapy etc.
Prevention is the gold standard and every efforts and care should be taken to prevent the diabetic foot by Optimal diabetes control, Effective local wound care, Infection control, Pressure relieving strategies, Restoring pulsatile blood flow. The limb salvage is the priority and this article highlights the pathogenesis, treatment options and preventive steps in this modern era.

Keywords: diabetic foot, neuropathy, vasculopathy, debridement, granulation tissue

Introduction
In the present age of Global village, non-communicable environmental diseases become a major public health concern. Urbanization, life style changes, socio cultural changes, pollution, increase in stress and tensions among people in the society are the contributory factors for the increase in the prevalence of non-communicable diseases [1]. Worldwide, above 75% of all deaths happens due to non-communicable diseases (NCDs). This is particularly more widespread in underdeveloped and developing countries, due to deprived health system. Diabetes mellitus is one among the most common non-communicable diseases [2].
All over the world for every 30 seconds one foot is amputated due to diabetes and 85% of this can be prevented if early detection and adequate care is provided. 25% of all diabetics patient will develop foot ulcerations in their life period. One third of diabetic patient will develop significant peripheral neuropathy and /or peripheral vascular done. One third of diabetic patient seek hospital admissions due to diabetic foot ulcer. The patients face an enormous cost burden for treating diabetes in developing countries like India. The onset of diabetic foot ulcer is not spontaneous, and many warning signs precede. "Diabetic gangrene is not heaven sent but is born"= said Dr. Elliot about 75 years ago. Predicting the factors leading to diabetic foot ulcer and its complication can inform health care professionals to selectively concentrate to prevent amputations [3]. Understanding the predictive factors leading to leg ulcer complication including amputation is paramount for prevention.

Indian Scenario - Diabetes Mellitus
There is a rapid progression of the Diabetes epidemic in India. Nearly 74 million people (8.8 % of people) of India are suffering from Diabetes mellitus, which is almost 15% of Global statistics. It is also expected to increase to 99.7 million by the year 2040 [4]. In India, the prevalence of Diabetes is more evident in the urban areas when compared to rural populations, where it is one-quarter that of urban population. China has the larger proportion of Diabetes with 128.3 million populations and India follows with about 74.07 million [5].
The mortality and morbidity rates are due to the associated complication and are the major threat of this disease. To minimize the trouble of the disease in India, suitable interventions need to be taken by the government and

private sectors.

The annual population-based incidence of a diabetic foot ulcer is estimated from 1.0% to 4.1%. However, in people with diabetes the lifetime incidence may be as high as 25%. The diabetic foot ulcer is the major predisposing factor for non-traumatic foot amputations and 85% of these amputations are preceded by an infection. Through implementation of an effective evidence-based prevention program, effective patient education, comprehensive foot ulcer treatment by a multidisciplinary team, and periodic surveillance the rate of amputation can be abridged by 49–85%. The potentially preventable amputations constitute 75% which are carried out in neuropathic feet with secondary Infections, it is estimated 20 among 100 diabetic Indians are undergoing lower limb amputation. The total expenditure for amputation ranges from 50,000 to 1 lakh.

Relative five-year mortality following amputations rises up to 68 %[6]. Recurrence is more common among patients with healed ulcer. The major increase in mortality is due to the occurrence of macro and microvascular complications including development of the non-healing ulcer. It was found that one in three people with Diabetes has peripheral neuropathy or peripheral vascular disease. The commonest reasons for hospitalization of Diabetic patients are due to their foot problems (30% of admission). The rough estimates point out that approximately 45,000 legs are amputated every year in India and this rate is progressively increasing. The factors that contribute to high prevalence are walking with the barefoot or inappropriate footwear, low literacy rate, low socioeconomic status, late presentation by patients, inadequate knowledge on diabetic foot care among primary care physicians and unscientific belief in alternative systems of medicine. The alteration in somatic and autonomic sensations, small muscle dysfunction due to motor neuropathy and narrowing of blood vessels are the major etiology of development of foot ulcer.

Tamilnadu scenario

The diabetic prevalence in Tamilnadu as per the study conducted by ICMR IS 9.6 percentage higher than the National average. The study area located in this state Kanyakumari district also has the higher prevalence of Diabetes as reported as 9.7%. Age-wise prevalence showed a higher percentage among the younger group, and by the time people reached 55 years, almost 50 per cent will develop diabetic Foot Ulcer.

The National Urban Survey conducted across the metropolitan cities of India reported similar trend: 11.7 per cent in Kolkata (Eastern India), 6.1 per cent in Kashmir Valley (Northern India),[6]11.6 per cent in New Delhi (Northern India), and 9.3 per cent in West India (Mumbai) compared with (13.5 per cent in Chennai (South India), 16.6 per cent in Hyderabad (south India), and 12.4 per cent Bangalore (South India).[7] At 53 deaths per 1,00,000 population, Tamil Nadu had the highest death rate from diabetes among Indian states, followed by Punjab (44) and Karnataka (42), all significantly higher than the national average (23). Limb loss results due to delay in wound healing, insufficient treatment of foot infection and bacterial resistance. Numerous trial blessing innovative and explorative researchers are being carried out on diabetic foot ulcers and the methods of curing them from time immemorial. [8] Foot ulcer management requires multidisciplinary approach, by health care specialists. Debridement, offloading, and infection control plays a major part in management of Diabetic foot ulcer. Management of underlying systemic illness, such as hypertension, hyperlipidemia, atherosclerotic heart disease, obesity, or renal disease, is essential. It is also necessary to treat the arterial insufficiency, infection with suitable antibiotics, offloading the area of the ulcer, and wound care. Though there have been many treatment options for diabetic ulcer, optimal results are yet to be obtained.

There are various strategies in wound dressing to facilitate wound healing. If the standard treatment fails to heal the Diabetic foot ulcer, supplementary and advanced treatment modalities would be required. They are comparatively effective and have minimal side effects [9]. They are collagen products (COL), biological skin equivalents (BSE), biological dressings (BD), silver products, intermittent pneumatic compression therapy (IPC), negative pressure wound therapy (NPWT), electromagnetic therapy (EMT), keratinocytes, platelet-derived growth factor (PDGF), platelet-rich plasma (PRP), hyperbaric oxygen (HBOT), topical oxygen, Honey dressing and ozone oxygen etc [10].

Pathophysiology

Atherosclerosis and peripheral neuropathy occur with increased frequency in persons with diabetes mellitus (DM).

Diabetes-Related Atherosclerosis

Overall, people with diabetes mellitus (DM) have a higher incidence of atherosclerosis, thickening of capillary basement membranes, arteriolar hyalinosis, and endothelial proliferation. Calcification and thickening of the arterial media (Mönckeberg sclerosis) are also noted with higher frequency in the diabetic population, although whether these factors have any impact on the circulatory status is unclear.

The pathophysiology of diabetic peripheral neuropathy is multifactorial and is thought to result from

- Vascular disease occluding the vasa nervorum
- Endothelial dysfunction
- Deficiency of myoinositol-altering myelin synthesis
- Diminishing sodium-potassium adenine triphosphatase (ATPase) activity
- Chronic hyperosmolarity, causing edema of nerve trunks
- Effects of increased sorbitol and fructose.

The result of loss of sensation in the foot is repetitive stress; unnoticed injuries and fractures; structural foot deformity, such as hammertoes, bunions, metatarsal deformities, or Charcot foot, further stress; and eventual tissue breakdown. Unnoticed excessive heat or cold, pressure from a poorly fitting shoe, or damage from a blunt or sharp object inadvertently left in the shoe may cause blistering and ulceration. These factors, combined with poor arterial inflow, confer a high risk of limb loss on the patient with diabetes.

Diabetic Peripheral neuropathy will have three component and all these three namely sensory.motor and autonomy neuropathy constitute for the formation of ulcer. The algorithm of Diabetic neuropathy causing foot ulcer are shown in fig1 (a),

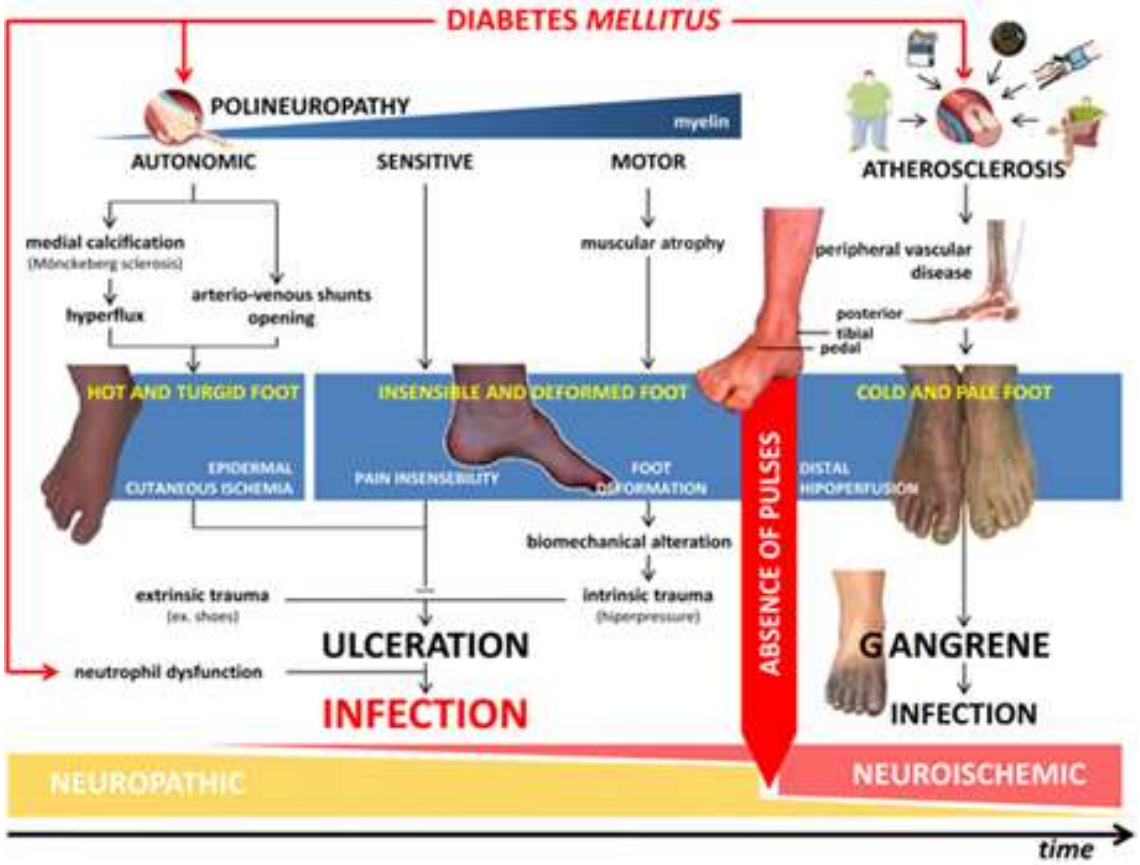

Fig 1: Diabetic Peripheral neuropathy causing Foot ulcer.

Staging and Classification of Diabetic Foot Ulcer

Staging and classification are important for

1. Assume the etiology
2. Predict this prognosis
3. Choose appropriate treatment
4. Monitor program
5. Serve as a form of communication

There are numerous classifications of Diabetic foot ulcer. Based on the etiology the diabetic foot ulcers are classified as

1. Neuropathic ulcer
2. Neuro Ischemic ulcer

Characteristic	Neuropathic Ulcers	Ischemic Ulcers
Patients age	Younger(fifth to sixth decades)	Older (seventh to eighth decades)
Pedal deformities	Hammer or claw toes, Charcot deformity	None
Skin	Warm with good colour	Cool, often red
Ulcer features	Wet with drainage, often located on pressure points of planter surface	Dry black eschar, often located on dorsal surface of feet and toes
Pulses	Intact	Diminished to absent
Pain	Often absent	Often painful

Fig 2: Neuropathy vs Ischemic ulcer

Wagner Magit classified based on depth and infection in to 6 grades. However this is not inter connected and hence ulcer with infection in the superficial ulcer will not be included in the classification is shown in figure3

Grade 0	Grade 1	Grade 2
No ulcer in a high risk foot 	Superficial ulcer involving the full skin thickness but not underlying tissues 	Deep ulcer penetrating down to ligaments and muscle but no bone involvement or abcess formation 
Grade 3	**Grade 4**	**Grade 5**
Deep Ulcer with cellulitis or abscess formation often Osteomyelitis 	Localized gangrene 	Extensive gangrene involving the whole foot 

Fig 3: Wagner Maggit classification

Factors Contributing Foot Ulceration

Multiple intrinsic and extrinsic factors contribute the formation of diabetic foot ulcer as shown in Table 1

Intrinsic factors	Extrinsic factors
▪ Bony prominences	▪ Walking barefoot
▪ Limited joint mobility	▪ Inappropriate footwear
▪ Deformities	▪ Falls and accidents
▪ Callus formation	▪ Objects inside shoes
▪ Previous foot ulcer	▪ Thermal trauma
▪ Neuroarthopathy (charcot)	▪ Activity level

Table 1: Factors contributing diabetic foot ulcer

With these intrinsic and extrinsic factors with neuropathy, vasculopathy and immune dysfunction results in diabetic foot ulcer.

Various Treatment Modalities

1. Wound Debridement

Never be kind with diabetic foot. All devitalized tissues must be removed till fresh bleeding come. Debridement can be done by

- Surgical
- Larva
- Hydrosurgery
- Autolytic
- Ultrasoni

Fig 4: A and B surgical debridement and Larva for wound debridement

Maggot debridement therapy (MDT) is an effective method for debriding wounds such as leg ulcers, supporting the concept of wound bed preparation. New evidence is emerging to suggest that maggots might contribute to wound healing by their properties in the reduction of biofilms and disinfection of wounds [15]. FDA-approved maggot debridement therapy (MDT), the application of sterile laboratory-reared *Lucilia sericata* (green bottle fly) larvae to wounds, is a cost-effective and successful treatment for diabetic foot ulcers and other medical conditions. [16].

2. Pressure off Loading

Pressure mitigation is the most important treatment in neuropathy ulcer. Either total contact last or diabetic air walker are used using Barometric study on dynamic and

static method the potential neuropathic ulcer patient cause be preventive by giving different pressure soles.

Fig 5: (a) (b) Pressure Offload

3. Phenytoin Powder Therapy

Phenytoin sodium is a Diphenyl substituted Hydantoin which is the most effective drug used in the treatment of epilepsy. Phenytoin as local dressing has been used by many workers because of its positive effects of therapeutic properties such as the increase in the proliferation of fibroblasts and deposition of collagen, Neovascularization, Enhanced granulation tissue formation, Decrease in the action of collagenase and bacterial contamination [12]. A number of clinical studies indicate that phenytoin decreases the bacterial load of wounds. Topical phenytoin was reported to eliminate Staphylococcus aureus, E. coli, Klebsiella spp. and Pseudomonas spp. from wounds within 7-9 days

4. Honey Therapy

From ancient times, honey has been used as a remedy for wound healing. But still, only limited supportive evidence are there to accept Honey as a medical property in wound healing. According to evidence found by the anthropologist, Egyptians had used this approach 5000 years' ago. The anti-bacterial activity *in vitro* and the supporting clinical studies show that application of honey clears severely affected infection. The possession of anti-inflammatory activity and stimulation of immune responses by honey are indicated in the research. The tendency to dehydrate bacteria due to its high acidity demonstrates the microbe killing ability of honey. In this era of raising antibiotic resistance, the antibiotic properties of honey are a useful alternative [13].

5. Platelet Rich Plasma

Autologous plasma concentrate delivers high concentration of growth factors in the wound. Growth factors in the PRP initiate chemotaxis, promotes proliferation and angiogenesis can be used as gel, powder preparation or local injections in and around the wound [14] The details of plasma preparation and results of PRP use are shown in figure 6(a) & (b)

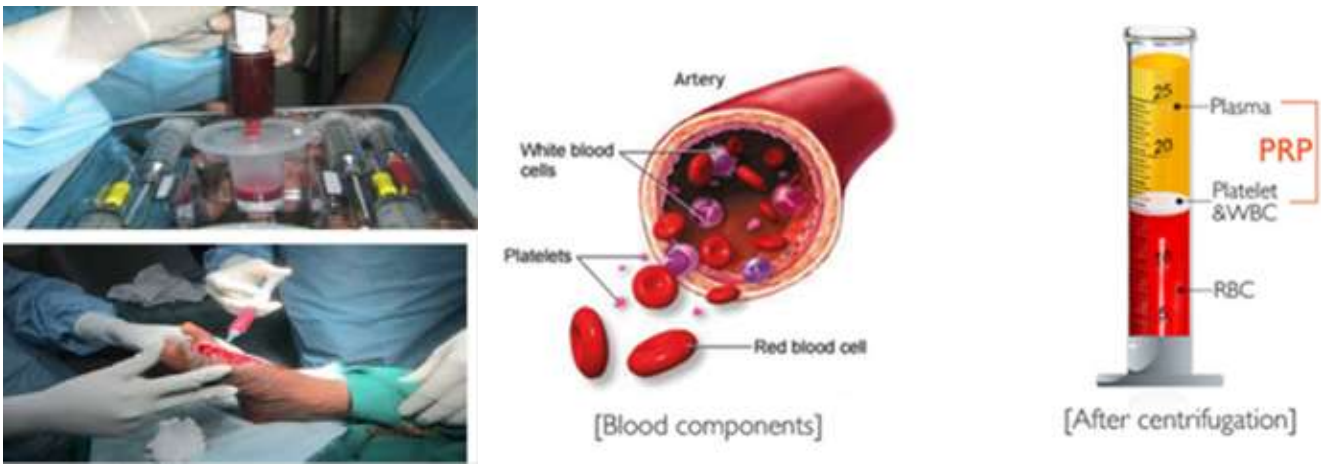

Fig 6: (a) and (b) Platelet rich Plasma

4: Epidermal Growth Factor

Recombinant Human epidermal growth factors initiates and promote healing in neuropathic foot ulcer when applied locally.[11] Epidermal growth factor (EGF) is a single chain polypeptide comprising 53 amino acids is playing a vital role in the wound healing by stimulating epidermal repair and proliferation of cells by inducing enhanced mitosis. In a chronic wound setting the growth factors will be decreased or inhibited, the proinflammatory cytokines and matallomatrix protein will be elevated. The replacement of these growth factors by means of local application or injection can enhance the wound healing [9].

Epidermal growth factors can modulate the pool of cytokines and convert the growth factors as the vascular endothelial growth factor and transforming growth factor - B1 (TGF-B1). TGF-β1 acts as a master by its effects on inflammation control, promoting fibroblast proliferation, angiogenesis, collagen synthesis, and increasing the influx and remodeling of the new extracellular matrix.

Thus, growth factors act as a rate limiting factor in diabetic

wound healing and due to its angiogenic activity promotes the growth of a vascular mesh within the wound bed.

5. Bone Marrow Aspirate

Bone marrow stem cells and progenitor cells are potential new
therapeutic option to induce angiogenesis. Bone marrow aspirate concentrate is made from fluid taken from bone marrow. The bone marrow aspirate contains stem cells that can help the healing of some bone and joint conditions. Bone marrow aspirate concentrate is obtained with a minimally invasive procedure that avoids the risks of an open bone graft procedure. The instruments and method shown in fig11.

Fig 7: Bone marrow aspiration

6. Hyperbaric Oxygen Therapy

Increasing the partial pressure of oxygen is the main therapeutic value of hyperbaric oxygen therapy. When a patient breathes pure oxygen at 3 times atmospheric pressure, arterial oxygen pressures in excess of 2000 mm/Hb are possible. This is around 20 times higher than normal· [17]. This is bactericidal to clostridium perfringens, stops toxin production in gas gangrene, and more rapidly displaces carbon monoxide from possible neurological damage.

Primary effects of HBOT:

- Vascoconstriction
- Angiogenesis
- Leucocyte oxidative killing
- Antibiotic properties
- Toxin inhibition

7. Negative Pressure Wound Therapy/Vac

VAC therapy applies sub atmospheric pressure to the wound tocreate an environment to promote wound healing by granulation tissue formation [18].

8. Direct Arterial Surgical Intervention

The angiosome concept of foot perfusion was conceived based on anatomical studies of arterial circulation and used for planning surgical procedures, tissue reconstruction, and amputation in order to achieve limb salvage... Its application is relevant in diabetic patients with critical limb ischemia and nonhealing amputation. The enhanced tools for accurate assessment of the lesion and area of involvement various direct surgical procedures are carried out [19].

Endovascular:

- Balloon angioplasty +/-stent
- Surgery:
- Bypass
- -Anatomical
- Aorto-bifemoral
- Ileo-femoral
- Femoro-popliteal
- -Extra-anatomical
- Axillo-bifemoral
- Femoro-femoral

Important factors that should be considered when planning the treatment are the number of affected angiosomes and CRP. Factors inhibit wound healing after revascularization [20].

Are

1. Location and extent of ischemic tissue defects
2. Systemic factors relating to wound healing ability / defence system
3. Infection
4. Inadequate topical treatment
5. Insufficient blood supply due to inadequate revascularization

Conclusion

Prevention is better than cure. All Diabetic foot patients must be given adequate counselling to take steps to prevent ulcerations**.**

Educate Patients on Proper Foot Care-The Do's

- Check your feet every day for cuts, cracks, bruises, blisters, sores, infections, unusual markings
- Use mirror to see the bottom of your feet if you cannot lift them up
- Check the color of your legs & feet-seek help if there is swelling, warmth or redness
- Wash and dry your feet every day, especially between the toes

- Apply a good skin lotion every day on your heels and soles. Wipe off excess.
- Change your socks every day.
- Trim your nails straight across.
- Clean cut or stratch with mild soap and water and cover with dry dressing.
- Wear good supportive shoes or professionally fitted shoes with low heels(under 5cm)
- Buy shoes in the late afternoon since your feet swell by then.
- Avoid extreme cold and heat(including the sun)
- See a foot care specialist if you need advice or treatment.

Do not

- Cut your own corns or callouses
- Treat your own in-growing toenails or silvers with a razor or scissors. See your doctor or foot care specialist
- Use over the counter medications to treat corns and warts
- Apply heat with hot water bottle or electric blanket – may cause burns unknowingly
- Soak your feet
- Take very hot baths
- Use lotion between your toes.
- Walk barefoot inside or outside
- Wear tight socks, garter or elastics or knee highs
- Wear over the counter insoles – may cause blisters if not right for your feet
- Sit for long periods of time
- Smoke

References

1. Mahmoud Ibrahim. Global Status of Diabetes Prevention and Prospects for Action: A consensus statement Diabetes Metabolism Research and review First published, 2018. https://doi.org/ 10.1002/dmrr.3021
2. Ogurtsova K. Global estimates for the prevalence of diabetes for 2015 and 2040 IDF Diabetes Atlas DOI: https://doi.org/10.1016/j.diabres.2017.03.024 June 2017; 128:40-50
3. Diabetes facts and figures IDF Diabetes Atlas 8th Edition, International Diabetic federation www. diabetes atlas.org
4. Sampath Kumar KP. Diabetes epidemic in India, A comprehensive review of clinical features, management and remedies, The Pharma Innovation publication. 2012; 1(2):16.
5. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. AMJ. 2014; 7(1):45-48. http//dx.doi.org/10.4066/AMJ.2014.1979
6. Mohan V. Epidemiology of type 2 diabetes: Indian scenario, Madras Diabetes Research Foundation &Dr Mohan's Diabetes Specialities Centre, Chennai, Indian Council of Medical Research, New Delhi & Office of the World Health, 2010.
7. Armstron DG Wrobe. "Are diabetes related wounds and amputations worse than cancer? International wound journal. 2007; 4(4):286-287 DOI 101111/j 1742-481x2007.00392x
8. Kannan Iyanar. Isolation and antibiotic susceptibility of bacteria from foot infections in the patients with diabetes mellitus, International Journal of Research in Medical Sciences. 2014; 2(2):457-460
9. Marwa Ahmed, Sherif A. Reffat Amany, Hassan Fikry Eskander. Platelet-Rich Plasma for the Treatment of Clean Diabetic Foot Ulcers Annals of vascular Surgery. 2017; 38:206-211 https://doi.org/10.1016/j.avsg.2016.04.023
10. Viswanathan Mohan, Siddharth Shah, Banshi Saboo Current Glycemic Status and Diabetes Related Complications Among Type 2 Diabetes Patients in India: 2 © supplement to JAPI, 2013, 61
11. Human epidermal growth factor enhances healing of diabetic foot ulcers. Diabetes Care. Tsang MW1, Wong WK, Hung CS, Lai KM, Tang W, Cheung EY, Kam G, Leung L, Chan CW, Chu CM, Lam EK. 2003; 26(6):1856-61.
12. Jayalal JA, Selwyn J Kumar. Efficiency of Topical Phenytoin on Healing in Diabetic Foot Ulcer: A Randomized Controlled Trial, International Journal of Scientific Study, 2015, 3(3). DOI: 10.17354/ijss/2015/276
13. Al-Hariri Mohammed. The local effects of honey on diabetic foot disorder. Pak J Physiol. 2013; 9:32-35. http://www.pps.org.pk/PJP/9-1/Hariri.pdf
14. Ramachandran, Current Status of Diabetes in India and Need for Novel Therapeutic Agents, Japi publication. 2010; 5:7-9.
15. Abela G. Benefits of maggot debridement therapy on leg ulcers: a literature review. Br J Community Nurs. 2017; 22(6):S14-S19. [PubMed] [Google Scholar
16. Linger RJ, Belikoff EJ, Yan Y. Towards next generation maggot debridement therapy: transgenic Lucilia sericata larvae that produce and secrete a human growth factor. BMC Biotechnol. 2016; 16(30):1-12. [PMC free article] [PubMed] [Google Scholar]
17. InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Type 2 diabetes: Does hyperbaric oxygen therapy help in the treatment of diabetic foot ulcers? 2018 Jan 11. Available from: https://www.ncbi. nlm.nih.gov/books/NBK481483/
18. Dalla Paola L. Diabetic foot wounds: the value of negative pressure wound therapy with instillation. *Int Wound J*. 2013; 10(1):25-31. doi:10.1111 /iwj.12174
19. van den Berg J, Pedal Artery C. Revascularisation: 'Bogey', 'Birdie', or 'Eagle' in the Treatment of Chronic Limb Threatening Ischaemia?European Journal of Vascular and Endovascular Surgery, 2019, 58.
20. Palena LM, Garcia LF, Brigato C.Angiosomes: how do they affect my treatment? Tech Vasc Interv Radiol. 2014; 17:155-169
21. Satinder Kaur, Gurjeet Singh, Lakhvir Kaur, Narinder Kaur, RK Dhawan. Diabetic Neuropathy: A Review. International Journal of Pharmaceutical Science and Research,2020:5(2):18-23.