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Original Article

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Impact of Myoinositol in Polycystic Ovarian Syndrome

Wajeeda Tabasum[1], Roya Rozati[2], Ayapati Gautam Mehdi[3], Humaira Minhaj[4], Taalia Nazeer Ahmed[5]

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Abstract

Polycystic ovary syndrome (PCOS) is one of the most common causes of infertility and metabolic problems among women of reproductive age. Myo inositol (MI) is administered in women with polycystic ovary syndrome (PCOS) over the last few years. It plays an important role in many metabolic pathways if the function is impact which affects the human health. Many hormonal and reproductive disorders associated with this disorder seem relieved by the supplement. The main symptom seems to be an increased androgen concentration, which in turn may contribute to different metabolic disorders which is improved in women with PCOS by supplementation of MI. Administration of MI is a safe and effective option to prevent and correct metabolic disorders in teenagers affected by PCOS. Thus, the aim of this review is to present the effectiveness of MI in the treatment for PCOS symptoms.

Keywords: Myo-inositol (MI); Polycystic ovary syndrome (PCOS); Insulin Resistance (IR).

INTRODUCTION

Myo inositol has been used to prevent and/or treat a number of metabolic disorders related to IR, such as the metabolic syndrome.[1] (Giordano D et al., 2011,[2] Santamaria A et al., 2012), gestational diabetes mellitus.[3] (Celentano C et al., 2016,[4] D'Anna R et al., 2015.[5] D'Anna R et al., 2013,[6] Santamaria A et al., 2015,[7] Zheng X et al., 2015,) and the polycystic ovary syndrome (PCOS).[8] (Genazzani AD et al., 2016.[9] Unfer V et al., 2012.[10] Unfer V et al., 2016)

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Polycystic ovary syndrome (PCOS) is a common endocrinopathies affecting in reproductive age which affects up to 20% of women. Polycystic ovaries on ultrasound, menstrual irregularity, and hyperandrogenism which can lead to acne, alopecia, hirsutism, insulin resistance, Itis associated with several other health complications such as Obesity,[11] (Lim SS et al., 2012, [12] Vrbikova J et al., 2009) obstetric Complications, infertility, (Palomba S, et al., 2015.) and early pregnancy loss characterize it.[13] (L. Vizza, et al., 2016,[14] Y. Suvarna et al., 2016,[15] A. B. Motta et v al., 2012) cardiovascular diseases,[16] (de Groot PCM et al., 2011,[17]. Rizzo M et al, 2009) Diabetes Mellitus Women suffering from PCOS have low fecundity with anovulation[13] (L. Vizza et al., 2016) and, to an extent, early pregnancy loss.[14] (Y. Suvarna et al., 2016) and pregnancy complications.[15] (A. B. Motta et aal., 2012). Induction of ovulation would restore ovulation and pregnancy. For many years clomiphene citrate (CC) has been the standard treatment for ovulation induction for these patients

The improvement of Insulin Resistance and reduction of circulating insulin are key therapeutic

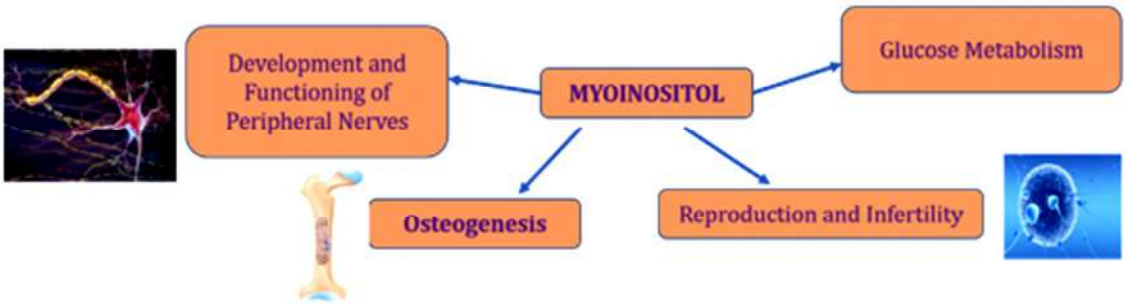
targets in PCOS enhancing fertility and reducing the lifelong risk for type 2 diabetes and early cardiovascular disease. MI is now considered as a insulinsensitizing supplement which could which improves insulin signaling, reduces serum insulin, and decreases serum testosterone, thereby restoring normal ovulatory function in PCOS women.[18] (Nestler JE et al., 2015.[19] Facchinetti F et al., 2015.[20] Costantino D et al., 2009.[21] Tang T et al., 2009)

ROLE OF MYOINOSITOL

Myo inositol (MI) and DCI are isoforms of inositol and belong to the vitamin B complex. Myo inositol is widely distributed in nature, whereas DCI, the product of epimerization of C1 hydroxyl group of MI, is relatively rare.[22] (Yoshida K et al., 2006)

Myoinositols play an Important role in cellular morphogenesis and cytogenesis. It helps in the synthesis of lipids, creation of cell membranes & cell growth. It Regulates, secretion of some exocrine glands such as pancreas & ovaries via signal transduction pathways.

Myoinositol Regulates calcium metabolism. It is involved in the release of cortical granules, Inhibition of polyspermy, Completion of meiosis and Activation of the cell cycle results in embryonic development.[23] (Papaleo 2009). It helps in calcium metabolism and oogenesis. At ovarian level it has been shown that MI based second messenger is involved in both glucose uptake and FSH signaling.



Picture 1: Depicts Importance of Myoinositol.

Role of Inositols in Ovulatory Function and Fertility In PCOS

MI treatment in patients with PCOS improved ovarian function and fertility.[24] [Raffone E et al., 2010], decreased the severity of hyperandrogenism, acne and hirsutism.[25] (Zacche MM et al., 2009.[26] Ciotta LII et al., 2010) and positively affected metabolic and hormonal parameters deeply involved in the reproductive axis function and ovulation.[27] (Artini PG et al., 2013). For these reasons, it became a novel method to improve spontaneous ovulation.[28] (GerliS et al., 2007) or ovulation induction. MI improves response to clomiphene citrate in infertile women, restores ovulation, and increases clinical pregnancy and live birth rate.[29] (Kamenov Z et al., 2015) quality of oocytes in IVF cycles.[30] (Unfer et al., 2011). MI would be helpful in adolescents with PCOS to prevent reproductive disorders in future.

Picture 2: Depicts the Benefits of myo-inositol on for human health.

Effect of Myo-Inositol on Polycystic Ovarian Syndrome

PCOS Symptom	Inositol	Effect
Androgen excess	MI	-Total and free Testosterone level reduction. (Costantino, D et al., 2009)[20]
		-Free Testosterone decrease; E2, SHBG increase. (Benelli, E et al., 2016) [31]
		-Testosterone level reduction. (Artini PGet al., 2013)[27]
Ovulation and fertility disorders; ovaries dysfunction		-Better development of mouse embryos. (Chiu, T.T.Y et al., 1992)[32]
		-Restored spontaneous ovulation; elevated rate of fertilization/pregnancy. (Nestler, J.E et al., 1999)[33]
		-Increased FSH sensitivity, better fertilization rates and embryo quality; reduced LH:FSH ratio. (Artini PG et al., 2013)[27]
		-Restored spontaneous ovarian activity and fertility. (Papaleo, E et al., 2007)[35]
		-Higher ovulation frequency, shorter time to first ovulation. (Gerli S et al.,2007)[28]
		Improved Menstrual cycle and Ovulation rate
Metabolic abnormalities		-Improved glucose-to-insulin ratio and HOMA index. (Artini PG et al., 2013)[27]
		-Increased circulating HDL level, weight loss, and leptin reduction. (Gerli S et al.,2007)[28]
		Improved insulin sensitivity
		Reduced BMI

Resistance to Myoinositol in PCOS Patients

Despite the very good effect of MI on metabolic, hormonal, and reproductive parameters of PCOS patients, 25% to 75% of them could be resistant to this treatment. The reason for this resistance is still unclear but could be related to the state of obesity, insulin resistance, and hyperandrogenemia or differences in compound bioavailability.

In one of the study published most of the patients resistant to MI were obese.[29] (Kamenov Z. et al. 2015) did not show increased plasma levels of MI.[36] (Oliva M et al. 2018). These MI resistant patients were treated in Combination of cc and myoinositol in non-ovulating or nonpregnant patients could be useful to achieve the goal of ovulation/pregnancy in Obese patients.

In patients who did not show increased plasma levels of MI were treated with a combination of MI and α lactalbumin, their plasma levels at the end of the treatment significantly improved compared to the baseline and were similar to the patients who responded positively to the treatment with MI alone.

DISCUSSION

Polycystic ovary syndrome is one of the most common endocrine disorders affecting women. MI is generally well tolerated across the range of therapeutic dosages.[37] (Carlomagno G et al., 2011), with the exception of minor side effects reported at higher concentration.

Myoinositol act as a mediator of insulin action, evidence has shown that myoinositol, may improve the hormonal profile, oxidative abnormalities and metabolic factors among PCOS women, probably due to amelioration of insulin resistance.[38] (Unfer V, et al.,2017) and helps in reduction of hyperandrogenism.[39] (Monastra G et al., 2017). Lifestyle modifications, including diet control and physical exercises, seem to be extremely important and should be the first-line of treatment in overweight patients with PCOS.[40] (Orio, F. et al., 2010) Some studies have shown promising results in women receiving myoinositol.[41] (Zheng X et al., 2017.[42] Showell MG et al., 2018) whereas Cochrane review published in 2018 could not draw any benefits of myoinositol among infertile PCOS women.[43] (Larner J et al., 2010). Few studies suggest that the effectiveness of MI in the treatment of hirsutism and other cutaneous disorders in young women with PCOS.[44,45] (Minozzi M et al., 2008 and 2011)

CONCLUSION

MI may prove useful in the treatment of PCOS patients undergoing ovulation induction, both for its insulin-lowering activity and its intracellular role in oocyte maturation. Myoinositol might be used alone as an insulin sensitizer to improve metabolic, hormonal and reproductive outcome in infertile PCOS women. MI showed promising results as a safe approach for the prevention and treatment of Gestational Diabetes Mellitus. myoinositol, the combination used could be beneficial for improving metabolic, hormonal, and reproductive aspects of PCOS.

Author Contributions: WT. and RR. designed the research. WT. performed the literature search, interpreted the data, and drafted the manuscript. WT., RR., A.G.M., H.M., and T.N.A. performed the literature search and made a critical revision of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

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Foot Macrodactyly: A Review

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Abstract

Macrodactyly affects the foot less frequently than the hand. Macrodactyly has yet to be identified as a cause. A gain-of-function mutation in the PIK3CA pathway causes this form of overgrowth. The two categories of clinical manifestations are static and progressive clinical symptoms. Anteroposterior (AP) measurements are taken on both feet. Young people should have soft tissue reductions, epiphysiodesis, epiphysectomies, osteotomies, and other treatments. Adults are more likely to use arthrodesis and shortening surgeries.The purpose of surgery is to reduce the size of the foot so that standard shoes can be worn and the cosmetic look can be improved.

Keywords: Macrodactyly; Foot.

INTRODUCTION

Macrodactyly of the foot is a rare congenital abnormality that causes pain, calluses[1], ulcers, difficulties wearing shoes, impairment in ambulatory capacity and gait development, aesthetic issues, and psychological issues.[2]

BACKGROUND

Macrodactyly affects the foot less frequently than the hand. One in every 18000 people is affected by primary macrodactyly, with a modest male predominance of.[3,4] Macrodactyly is also known as megalodactyly, macrodystrophia lipomatosa, macrodactyly fibrolipomatosis, lipomatous overgrowth or hamartoma, gigantomegaly, local gigantism, and digital gigantism. The second ray is usually the first, followed by the third, then the first, fourth, and fifth.[5]

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ETIOLOGY

The cause of macrodactyly has yet to be discovered. Improper finger irrigation, abnormal humoral mechanism, and abnormal innervation are all possible reasons (the last two causes are not well demonstrated, the first one because the nerves exert great control over the growth).

PATHOGENESIS

An overgrowth condition is caused by a gain of function mutation in the PIK3CA pathway (Phosphatidylinositol - 4, 5 - Bisphosphate 3-Kinase).[6,7] For normal cell growth, metabolism, and survival, the PI3K/AKT/mTO Rsignalling pathway is essential. Cancer and the PIK3CA-

Related Overgrowth Spectrum, a collection of overgrowth illnesses, can be caused by somatic mutations in this system (PROS). PIK 3 CA SNPs in PROS generate asymmetric overgrowth by promoting physiologically inappropriate activation of AKT and mTOR. This includes disorders like macrodactyly, CLOVES (Congenital Lipomatous Overgrowth, Vascular Malformation, Epidermal nevi, Spinal/skeletal Anomalies), hemimegalencephaly, and others. Because these mutations are postzygotic, they are only found in some cells and not others.

PATHOLOGY

Subcutaneous fat in adults looks like proliferative adipose tissue. (Image 1) Fat lobules are large, dark, and difficult to remove. The digital nerve has expanded in size, with an increase in fat and fibrous tissue seen in a cross section. The digital artery wall thickness is normal. Blood vessels, tendons, and the sheaths that surround them are normally untouched. As a result, the blood supply fails to keep up with the toe's growth, resulting in vascular insufficiency. The phalanges' medullary canals are always larger, and fatty marrow is apparent.

Patients with diagnoses of other known overgrowth syndromes or otherwise uncharacterized syndromic presentations of lower extremity enlargement were excluded, as were patients with Klippel Trenaunay syndrome, Proteus syndrome, CLOVES syndrome, Ollier's disease, Maffucci syndrome, Milroy's disease, neurofibromatosis, and vasculaanomalies.

TYPES OF CLINICAL MANIFESTATION

According to Barsky, there are two types of clinical manifestations: the static form, in which the finger is larger from birth but grows proportionally with the rest of the fingers, and the progressive form, in which the finger is normal at birth but begins to grow faster than the rest of the fingers, causing angular deviation.[8] For examples described in the hand[9], however, De Laurenzi identified the less common progressive type.

The condition manifests itself unilaterally in 95% of cases. It appears in a decreasing order from the great toe to the fifth toe in males and is slightly more common in females. In the progressive form, the toe stops growing when the epiphyses close, the sensitivity is usually normal, mobility declines over time, and bud ulcers are common.

Macrodactyly is associated with syndactyly in 10% of people[10], and polydactyly and cryptorchidism in a lower percentage. Klipper Syndrome is a condition that occurs when a person Maffuci Syndrome (multiple hemangiomatosis), Proteus Syndrome (hamartomatous dysplasia, pigmented nevi, and subcutaneous tumours), hemangiomas, arteriovenous malformations, congenital lymphedema, lipomas, osteoid osteoma, and melorrestos[11] Hernia may be linked to Macrodactyl.

The innervations of the medial plantar nerve were more pronounced in the affected toes and forefoot than those of the lateral plantar nerve. The clinical and anatomic aspects of foot macrodactyly were comparable to the affected digits primarily located in the area of the median nerve in hand macrodactyly, indicating that it was "nerve territory-oriented."[12,13] Enlargement, fatty infiltration, tortuosity, or a combination of these pathologic alterations are all examples of pathologic changes.[14] The remarkably consistent distribution of the nerve abnormalities and tissue hypertrophy suggested that macrodactyly of the foot was caused by nerve-mediated expansion.[15]

INVESTIGATION

We took standing anteroposterior (AP) and oblique radiographs of both feet and evaluated the range of motion of the metatarsophalangeal joint on the first visit (MTPJ). In standing anteroposterior radiographs, evaluate the intermetatarsal breadth and forefoot area on AP radiographs (Fig. 1 and 2).

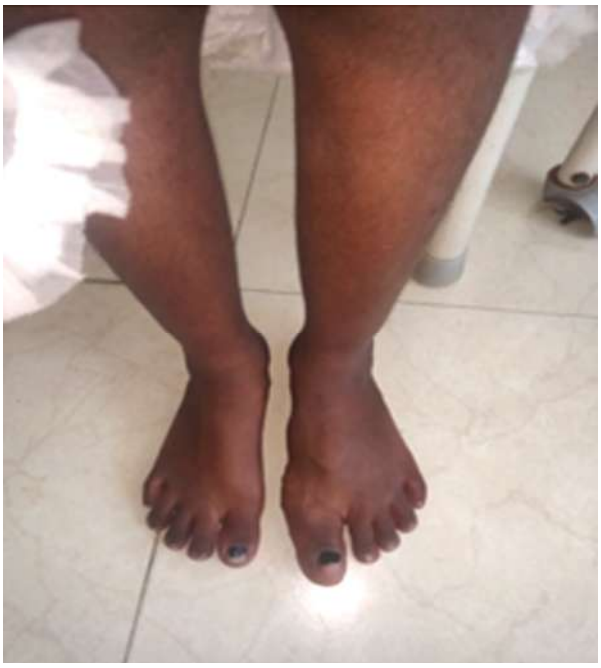

Fig. 1: Enlarged left big toe.

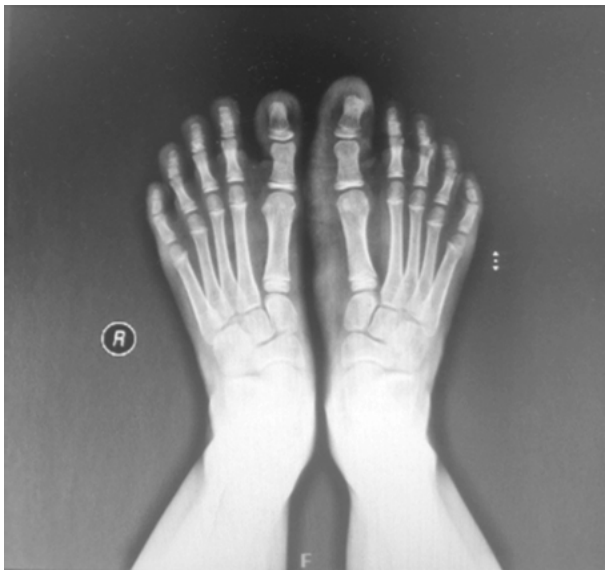

Fig. 2: Standing Antero posterior view of both foot.

We drew a line on the anatomical axis of the first metatarsal and labelled the point of intersection with the distal end of the first metatarsal as M1 to calculate the inter metatarsal breadth. A similarly generated point on the fifth ray was given the designation M5. The distance between M1 and M5 was used to compute the intermetatarsal breadth.The area of the soft tissue shadow distal to the tarsometatarsal joint was calculated using Image J software (NIH, Bethesda, Maryland) and recorded as the forefoot area. We measured these two radiographic parameters in the contralateral, normal foot and calculated the intermetatarsal width ratio as the intermetatarsal width of the macrodactylic foot divided by that of the normal foot, and performed a similar calculation with the forefoot areas of both feet to derive the forefoot area ratio.

Although the forefoot area, as a two dimensional measurement, is superior to a one dimensional measurement, such as foot length or foot breadth, a three dimensional CT or MRI could be used to quantify the volume of the foot prior to surgery.

To determine the nerve involvement, a nerve conduction examination is performed.

TREATMENT AND MANAGEMENT

The goal of surgery is to reduce the size of the foot so that it may be used in regular shoes and the appearance can be enhanced. Young people should have soft tissue reductions, epiphysiodesis, epiphysectomies, osteotomies, and other treatments. Adults[16-21] are more prone to undergo shortening operations and arthrodesis. Surgical indications for ray amputation, as previously stated by Bulut et al., were metatarsal involvement, joint immobility, or involvement of several digits.[22] Because the immobile macrodactylic toe impairs foot function, this is the case.

Hop and van der Biezen[23] described three cases of foot macrodactyly involving several digits and recommended amputation of the most swollen ray, shortening the adjacent ray, ray transposition, and soft-tissue debulking.

Kotwal operated on 21 cases and after 9 years of follow-up, the aesthetic aspect of the finger was good only in 57% of patients. The techniques used were two-stage soft tissue reduction and phalangectomy.[24]

When the metatarsal spread angle is raised by 10° relative to the normal side, or toe amputation would create a broad, cosmetically unattractive interphalangeal area, ray resection of the lesser toes should be performed. Because removal of the first ray is not suggested, treating macrodactyly of the great toe may necessitate many surgical procedures. After a comprehensive examination of the malformation, the surgeon can perform certain procedures on the child while he or she is still young.

After macrodactyly reconstruction techniques, complications are fairly common. Cutaneous necrosis is the most common, and it can be severe enough to jeopardise the toe's viability. After soft tissue reduction, 25 percent of patients developed cutaneous necrosis, according to Kostakoglu18. Dell also found this complication frequently after reconstruction techniques.[25]

Despite years of experience treating this difficult congenital defect, most individuals require many surgical operations during childhood, and a large percentage of them have an ugly and useless finger as a result.[26,27]

CONCLUSION

We may conclude that macrodactyly is a rare and complicated illness with a wide range of treatment options and frequent complications.

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Review Article

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Guidelines in Management of Necrotising Fasciitis

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Abstract

Necrotising fasciitis is a infection of subcutaneous tissue and fascia which may spread fulminantly to deeper tissues and wider tissues may cause damage severe damage to the tissues and present as a localised infection and fulminant septic shock with high mortality rate. In this Review, we will discuss about the current understanding and various guidelines in management of necrotising fasciitis.

Keywords: Necrotising fascitis; Guidelines; Surgical interventions.

INTRODUCTION

Necrotizing fasciitis is a frequent acute infection that affects people all over the world. The infection is usually caused by a post-traumatic, immuno-compromised patient. Edema and necrosis of subcutaneous tissues with involvement of neighbouring fascia, as well as painful red puffy skin over afflicted areas, are signs of a severe soft tissue infection caused by bacteria. Clinical symptoms of fulminant tissue destruction, systemic signs of toxicity, and significant mortality define these illnesses. Early surgical intervention and antibiotic medication are required for accurate diagnosis and proper treatment. We shall evaluate the role of several guidelines in the management of necrotizing fascitis in this review study.

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BACKGROUND

Hippocrates initially characterised Necrotising fasciitis about 500 BC, when he presented a clinical description of an erysipelas illness consequence that resembled the current description of Necrotising fasciitis. In 1783, Claude Colles, chief surgeon of the Hotel Dieu in Lyon, described a condition that resembled modern descriptions of necrotizing fasciitis.[1,2] Joseph Jones, a military surgeon in the Confederate States of America's army, was the first to describe contemporary Necrotising fasciitis. In 1883, Jean Alfred Fournier described a situation in which five males developed necrosis of the perineum; this kind of necrotizing fasciitis was named after him and is today known as Fournier's gangrene.Meleney found a link between beta-hemolyticstreptococcus A and a series of hospitalised cases in Beijing in 1924. Meleney's gangrene was the name given to these patients for several decades after that. Wilson proposed the term "necrotizing fasciitis" as a more precise description of this condition in 1952. The condition

was popularised as "flesh-eating bacterium syndrome" by the media.

AETIOLOGY AND RISK FACTORS

All standards imply trauma as the most common identifiable aetiology. The majority of patients had had minor or major traumas in the past, most of which were external injuries and surgical wounds. Among the most common causes of complicated intra-abdominal infections that can lead to Necrotising fasciitis are appendicitis with perforation, infection following the repair of an incarcerated hernia, perforated diverticulitis, necrotic cholecystitis, gastro-duodenal perforation, small bowel perforation, and obstructive colon cancer with perforation. The incidence of necrotizing fasciitis caused by a surgical wound in the chest wall is higher than that of similar wounds in the lower abdomen wall. Such situations carry a high risk of osteomyelitis, which raises the patient's mortality rate significantly. Perianal abscess, surgical wounds, skin abscess drainage, and pressure sores are all common causes of Fournier's gangrene. Anorectal infection, ischiorectal abscesses, and colon perforations can all cause it as a consequence of colorectal illness. Another cause could be a urethral stricture or a trauma caused by an indwelling Foley catheter. It's frequently linked to Bartholin abscesses or vulval skin infections in women. In Asia, Necrotising fasciitis can be caused by eating raw or undercooked seafood or being bitten by fish fins.[2,3]

Risk factors for Necrotising Fasciitis Include

- Major penetrating trauma.[2,3]
- Minor laceration or blunt trauma (muscle strain, sprain, or contusion)
- Skin breach (varicella lesion, insect bite, injection drug use)
- Recent surgery (including colonic, urologic, and Gynaecologic procedures as well as neonatal circumcision)
- Mucosal breach (Haemorrhoids, rectal fissures, episiotomy)
- Immunosuppression (diabetes, cirrhosis, neutropenia, HIV infection)
- Malignancy
- Obesity
- Alcoholism
- In women: pregnancy, childbirth, pregnancy loss, gynecologic procedures

Types of Necrotising Fasciitis

Necrotising Fasciitis will be divided into four types based on the guidelines.[1,2,3]

Table 1: Types of Necrotising fascitis.

Types	Organisms	Regions Involved	Comorbids
I (Polymicrobial)	Obligate and facultative anaerobes	Trunk and perineum	Diabetes mellitus
II (Monomicrobial)	GroupA-beta haemolytic streptococcus		
III	Gram negative bacteria	Limbs , Trunk	Post traumatic
IV	Candida, Zygomycetes	Limbs, Trunk, perineum	Immunos uppression

Necrotising fasciitis is a type of infection caused by bacteria such as Vibrio spp. and Aeromonashydrophila, which are widely found in raw seafood and are referred to as "marine bacteria."

SIGNS AND SYMPTOMS

Clinical manifestations of necrotizing infection include.[2,3,4]

- Erythema (without sharp margins; 72%)
- Edema that extends beyond the visible erythema (75%)
- Severe pain (out of proportion to exam findings in some cases; 72%)
- Fever (60%)
- Crepitus (50%)
- Skin bullae, necrosis, or ecchymosis (38%)

Fever (102-105°F), tachycardia, and systemic toxicity are all possible side effects. Hypotension may be apparent at first or develop as the infection progresses. Malaise, myalgia, diarrhoea, and anorexia are some of the other symptoms. Gas is frequently discovered in the deep tissues of these mixed infections, much as it is in clostridia infections. Clostridium perfinges, Clostridium septicum, Clostridium histolyticum, and Clostridium novyi produce gas gangrene, which is a rapidly progressing infection.[2,3]

DIAGNOSIS

The results of laboratory tests are usually nonspecific. Acidosis, coagulopathy, hyponatremia, raised inflammatory markers (C-reactive protein and/or erythrocyte sedimentation rate), and

elevations in serum creatinine, lactate, creatine kinase (CK), and aspartate aminotransferase (AST) concentrations are some of the abnormalities that can occur.[2,3] Increased serum CK or AST levels indicate a deep infection involving muscle or fascia (as opposed to cellulitis). NSTI cannot be consistently predicted using laboratory measures, especially in the early stages of infection. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score[4] was developed using laboratory indicators such as white cell count, haemoglobin, sodium, glucose, creatinine, and C-reactive protein. Blood cultures are positive in about 60% of patients with monomicrobial (type II) necrotizing fasciitis caused by GAS or other beta-hemolytic streptococci, and they are consistently positive in necrotizing myositis patients. Blood culture yields are lower in patients with polymicrobial (type I) necrotizing fasciitis; in one study, it was just 20%. Furthermore, blood culture findings may not accurately reflect all organisms present.

LRINEC SCORING4

Table 2 : Lrinec Scoring.

Laboratory Risk Indicator for Necrotizing Fasciitis

CRP (mg/dL)	<15	0
	≥15	4
WBC (per mm3)	<15	0
	15-25	1
	>25	2
Hemoglobin (g/dL)	>13.5	0
	11-13.5	1
	<11	2
Sodium (mEq/dL)	≥135	0
	<135	2
Creatinine (mg/dL)	≤1.6	0
	>1.6	2
Glucose (mg/dL)	≤180	0
	>180	1
Composite Score	Score < 6	Low Risk
	Score 6-7	Intermediate
	Score ≥8	High Risk

ROLE OF IMAGING

A computed tomography (CT) scan is the finest initial radiographic imaging evaluation. The presence of gas in soft tissues, which is most commonly seen in the setting of clostridial infection or polymicrobial (type I) necrotizing fasciitis, is the most useful finding. This finding is highly specific for NSTI and should require early surgical intervention. Fluid collections, the absence or variability of tissue enhancement with intravenous contrast, and inflammatory alterations underneath the fascia are all possible radiography findings. For detecting gas in soft tissues, magnetic resonance imaging (MRI) is less effective than computed tomography (CT). Furthermore, MRI is extremely sensitive, overestimating deep tissue involvement and hence unable to effectively discriminate between necrotizing cellulitis and deeper infection.[6] Ultrasound can detect isolated abscesses and gas in tissues, although it hasn't been thoroughly researched in necrotizing fasciitis.

MEDICAL MANAGEMENT

Adults

- 4 g + 500 mg piperacillin-tazobactam (IV) every 6 hours and
- Clindamycin (IV) 900 mg every 8 hours 2,3,4.
- Ceftriaxone (IV): 2 g once a day and Metronidazole (IV): 500 mg every 8 hours can also be used if Streptococcus Pyogenes has been ruled out.

If MRSA is detected, each of the above-mentioned methods should be supplemented with Vancomycin (IV) 15-20 mg/kg every 12 hours.

Children

1. Piperacillin-Tazobactam (IV): 100 mg/kg piperacillin component per dosage, given every 8 hours.
2. Clindamycin (IV)

- Neonates: 5 mg/kg each dose, administered every 8 hours;
- Children's dose: 10 mg/kg, administered every 8 hours.

If Streptococcus pyogenes has been ruled out Ceftriaxone (IV): 80 mg/kg per dose, once a day and metronidazole (IV) can also be used:

- ***Neonates:*** 7.5 mg/kg per dose, administered every 12 hours
- ***Children:*** 7.5 mg/kg per dose, administered every 8 hours

If MRSA is suspected Vancomycin (IV) should be added to both of the above-mentioned options as follows

- ***Neonates:*** 15 mg/kg per dose, given every 12

hours

- ***Children:*** 15 mg/kg per dose, given every 8 hours.

Intravenous immunoglobulin can be considered in cases of severe necrotizing fasciitis, although efficacy has not been proven.

SURGICAL MANAGEMENT

Primary treatment of necrotizing fasciitis is early aggressive surgical exploration and debridement of necrotic dead tissue with recommended antibiotics coverage is mentioned in all guidelines.

Surgery: Extensive Wound Debridement (Fig. 1) is associated with appropriate broad-spectrum intravenous antibiotic therapy. During wound debridement, extensive debridement of dead tissues that cross beyond the area of involved tissues are needed. The wound should be left open post debridement and the wound re-inspected 24 hours later to assess the adequacy of the initial wound debridement. Antibiotic therapy is depends on gram stain and culture tests. If group A streptococcus is confirmed to be the cause, high dose penicillin or ampicillin and clindamycin, which blocks toxin production must be given.[4]

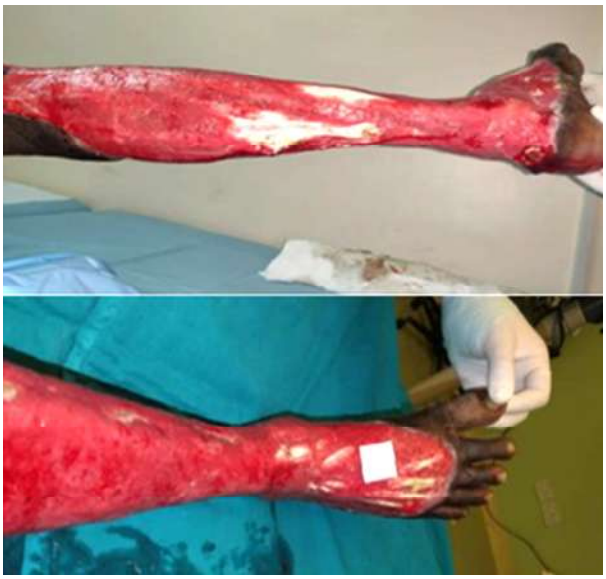

Fig. 1: Post debridement of the excision of the necrotic tissues should extend until healthy tissue is found, but should be limited to the edges of the infection

VAC therapy (Fig. 2) can be used for the superchargerd granulation of the wound after initial wound debridement to remove the exudates and necrotic sloughs from the wound.

Fig. 2: Vaccum Therapy in Necrotising Fascitis.

WOUND COVER

Skin grafts were the most commonly used wound cover surgery commonly used all over the world with easier postoperative care (Fig. 3, 4, 5). Loco-regional flaps like Reverse Sural artery flaps in lower extremities were also used. Free flaps especially muscle flaps plays a important role in post necrotising fasciitis reconstruction with wound having exposed tendons and bones.

Fig. 3: Post Debridement of Necrotising Fascitis

Fig. 4: Post Skin Grafting Day 10

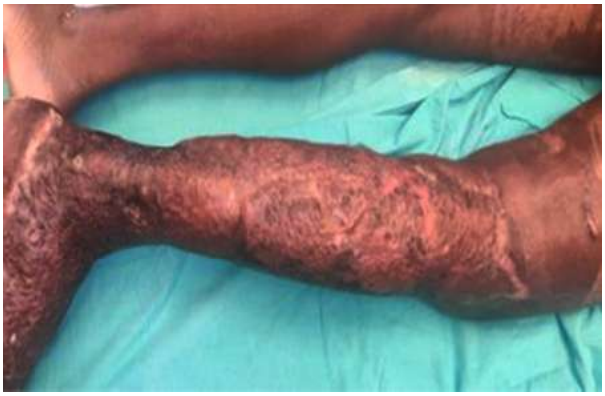

Fig. 5: Post Skin Grafting Day 30

Necrotizing fasciitis of the posterior neck raw area are covered using a Bilobedfasciocutaneous flap for repair following wound debridement. The blood supply of the bilobedfasciocutaneous flap originates from a row of musculocutaneous perforators of posterior intercostal arteries.[5]

The V-Y islanded fasciocutaneous flap, used to cover the urogenital region after necrotizing fasciitis wound debridement, is considered a option. The V-Y axial-pattern design of the flap is also considered a new option, which enabled the flap to be advanced and fashioned in the midline. The idea of using the V-Y-plasty design is popularised because the perineum has a pair of symmetrical anatomic structures. This procedure preserves tissue and the flap donor site is closed primarily without tension. Both aesthetic and functional results were satisfactory.[6] Free flaps like anterolateral thigh flaps, Lattismusdorsi flaps can be used for defects post debridement.[7]

Scrotal skin loss can occur following trauma, Fournier's gangrene, post tumour excision, burns for which there are techniques including residual scrotal skin mobilization, skin grafts, pedicle and free flaps. The management is complex due to the multiplicity of flaps and techniques. The Modified pudendal thigh flap used to reconstruct scrotal defects. This pedicle flap is reliable and produces a neo-scrotum that will be natural in appearance, good quality skin cover and cushion to the testes as well as protective sensation.[8]

CONCLUSION

Necrotizing fasciitis is a rare but life threatening condition, with a high mortality rate (mortality 32.2%) that approaches 100% without interventions. Comorbid conditions associated with this pathology, such as diabetes mellitus, immunosuppression, chronic alcohol disease, chronic renal failure, and liver cirrhosis, which can aggrarvate the rapid spread of necrosis, and increase in the mortality rate. The diagnosis of NF is difficult and the differential diagnosis between NF and other necrotizing soft tissue infections is difficult. However, the clinician should do their maximum effort to secure the diagnosis of NF, as a delay in diagnosis can be fatal to the patient. The early clinical picture includes erythema, swelling, tenderness to palpation, and local warmth, once the infection develops, the infection site develops skin ischemia with blisters and bullae. The diagnosis of NF can be faster with the use of scoring systems, such as the LRINEC score or the FGSI score, especially in cases of Fournier's gangrene. The diagnosis is definitely established by doing explorative surgery at the infected site. Management of the infection begins with antibiotic treatment. In the majority of cases with NF (70–90%) the pathogens are two or more, suggesting the use of broad-spectrum antibiotics. The value of antibiotic treatment in NF is relatively low, and early and aggressive drainage and debridement is required. In NF of the extremities, the clinician should consider amputating the infected limb if there is aggressive involvement. Finally, postoperative management of the surgical wound is important, along with proper nutrition of the patient. The use of VAC therapy in wound management has greatly improved the results of postoperative management.

Conditions Included in the Differential Diagnosis Include4

- ***Cellulitis***: Cellulitis presents with skin erythema, edema, and warmth. Fever may be present, but cellulitis is generally not associated with hemodynamic instability or exquisite tenderness. Elevations in serum CK or AST concentrations suggest deep infection involving muscle or fascia (as opposed to cellulitis).

- ***Pyodermagangrenosum:***Pyodermagangrenosum may be challenging to distinguish from necrotizing fasciitis. The diagnosis is important because unnecessary surgical debridement of pyodermagangrenosum can cause extension of the lesion, and inappropriate usage of immunosuppressive therapy may worsen necrotizing fasciitis.
- ***Gas Gangrene (clostridialmyonecrosis):*** Gas gangrene (clostridialmyonecrosis) is an acute invasion of healthy tissue that occurs spontaneously or as a result of traumatic injury. Both gas gangrene and polymicrobial (type I) NSTI are diagnosed with gas in the tissues. In gas gangrene, the Gram stain usually demonstrates gram-positive rods, while, in polymicrobial necrotizing fasciitis, the Gram stain usually demonstrates mixed aerobes and anaerobes. The difference is important in that management of clostridialmyonecrosis may require amputation, whereas management of necrotizing fasciitis needs debridement (but limb salvage may be possible).
- ***Pyomyositis:*** Pyomyositis may be confused with necrotizing myositis. These conditions differ in that pyomyositis is defined by abscess formation in skeletal muscle, while necrotizing myositis is characterized by gangrenous necrosis. These are distinguished by clinical and radiographic features. Pyomyositis is caused by S. aureus and is usually associated with less systemic toxicity than necrotizing myositis.
- ***Deep venous thrombosis:*** Deep venous thrombosis (DVT) is characterized by extremity swelling, pain, and warmth; the pain is less extreme compared to the necrotizing infection. Fever may be present in DVT but is more common in the soft tissue infection.

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- Abbreviations spelt out in full for the first time. Numerals from 1 to l0 spelt out
- Numerals at the beginning of the sentence spelt out

Tables and figures

- No repetition of data in tables and graphs and in text.
- Actual numbers from which graphs drawn, provided.
- Figures necessary and of good quality (color)
- Table and figure numbers in Arabic letters (not Roman).
- Labels pasted on back of the photographs (no names written)
- Figure legends provided (not more than 40 words)
- Patients' privacy maintained, (if not permission taken)
- Credit note for borrowed figures/tables provided
- Manuscript provided on a CDROM (with double spacing)

Submitting the Manuscript

- Is the journal editor's contact information current?
- Is the cover letter included with the manuscript? Does the letter:

1. Include the author's postal address, e-mail address, telephone number, and fax number for future correspondence?
2. State that the manuscript is original, not previously published, and not under concurrent consideration elsewhere?
3. Inform the journal editor of the existence of any similar published manuscripts written by the author?
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