



IMPETIGO IN THE PEDIATRIC POPULATION

Mohammed Abdullah Salawi¹, Rawan Fuad Habib², Moatez Khalaf Almofarreh³,
Shaimaa Ali Alghamdi⁴, Eyad Muslih Alnajrani⁴, Hajer Mohammad Aldeabel⁵, Eman
Hamdan Alghamdi⁵, Azam Abdulrahem Althqafi⁶, Saqer Mahl Althyabi⁷, Bandar
Abdullah Alqahtani⁸, Abdullah Salah Alswat⁹

¹Jazan University, ²Ibn Sina National College, ³Aljouf University, ⁴King Abdulaziz University

⁵Imam Abdulrahman Bin Faisal University, ⁶Umm Al-Qura University, ⁷Medical Services Of
Ministry Interior (Civil Defence), ⁸King Khalid Hospital, ⁹Taif University

Abstract:

Introduction: Normal healthy skin is usually colonized by a huge amount of bacterial organisms that inhabit the skin as commensal flora both on the surface of the skin or in the hair follicles. However, abnormalities in the growth and replication of these organisms (like overgrowth) can lead to the development of dermatological diseases where the same commensal organism can be responsible for the development of the disease. These commensal bacteria have the ability to create biofilms, which are sessile, complex accumulations of the bacterial organism along with a polymeric substance present extracellularly.

Aim of work: In this review, we will discuss the most recent evidence regarding the recent advances in the management of impetigo in the pediatric population.

Methodology: We did a systematic search for the recent advances in the management of impetigo in the pediatric population using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). Our search also looked for presentation, most common pathogens. All relevant studies were retrieved and discussed. We only included full articles.

Conclusions: Impetigo is considered to be the most common skin infection that affects children between 2-5 years old. It generally has two types: non-bullous (which is responsible for about 70% of cases) and bullous (which is responsible for the remaining of cases). Non-bullous impetigo can be caused by both staphylococcus aureus and streptococcus pyogenes. It is mainly distinguished by the presence of honey crusts on the face and limbs. Bullous impetigo, on the other hand, is only caused by staphylococcus aureus and results in the development of large bullae and blisters. It generally effects intertriginous body sites. Most cases of impetigo can resolve spontaneously within few weeks, regardless of the type of impetigo, and the development of late complications is usually rare. Treatment of impetigo is usually done using either topical or systemic antibiotics. Topical antibiotics are usually preferred in mild non-complicated cases due to their efficacy and safety. On the other hand, systemic treatment is preferred in more severe or complicated cases. Systemic antibiotics is sometimes challenging due the increasing rates of antimicrobial resistance.

Key words: Impetigo, children, presentation, management.

Corresponding author:

Mohammed Abdullah Salawi,
Jazan University

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INTRODUCTION:

Normal healthy skin is usually colonized by a huge amount of bacterial organisms that inhabit the skin as commensal flora both on the surface of the skin or in the hair follicles. However, abnormalities in the growth and replication of these organisms (like overgrowth) can lead to the development of dermatological diseases where the same commensal organism can be responsible for the development of the disease [1]. Generally, the bacterial flora of the skin includes mostly *Corynebacterium spp* (diphtheroids, aerobic), *Propionibacterium acnes* (diphtheroids, anaerobic), and *Staphylococcus epidermidis* (staphylococci, coagulase negative). More recent studies that used genetics and molecular biology techniques have also detected the presence of significant amounts of *Janthinobacterium spp* and *Pseudomonas spp* organisms in healthy skin [2].

These commensal bacteria have the ability to create biofilms, which are sessile, complex accumulations of the bacterial organism along with a polymeric substance present extracellularly. When they create biofilms, bacterial organisms have up to five hundred times the resistance to antimicrobials when compared to bacteria without biofilms. This is because that the biofilms increase the virulence of the bacteria and decrease their sensitivity to antibiotics.

Generally, newborns are aseptically with no commensal flora in their skin. Colonization of the bacteria starts usually within the first 14 days of their life. Many factors play a role in increasing the resistance of the newborn against infections and these include the presence of an intact skin, having acidic pH, the presence of sufficient sebaceous fatty acids and oleic acid, functioning lysosomes, defensins production, and proper state of nutrition [3].

On the other hand, many factors are associated with significant increases in the risk of developing skin infections. These include maceration, increased humidity, the presence of skin lesions, overweight, the use of corticosteroids, treatment with chemotherapeutic agents, dysglobulinemias, the presence of disorders of the WBCs like leukemia, diabetes mellitus, poor nutritional status, immunodeficiencies (both acquired and congenital), along with other risk factor.

Most bacterial organisms have the ability to grow on neutral pH skin with normal body temperature. Therefore, handwashing with regular soap led to significant declines in the incidence and prevalence of skin infections and systemic infections, especially

among children and their caretakers. In fact, a study has found that increasing the awareness on the importance of handwashing was associated with a 34% reduction in impetigo incidence [4].

In this review, we will discuss the most recent evidence regarding the recent advances in the management of impetigo in the pediatric population.

METHODOLOGY:

We did a systematic search for the recent advances in the management of impetigo in the pediatric population using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). Our search also looked for presentation, most common pathogens. All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: Impetigo, children, causes, presentation, and management.

STREPTOCOCCI'S CHARACTERISTICS:

Streptococci is usually classified using the Lancefield classification, which depends mainly on the C antigen that is present in the cell wall, and classifies the organism into groups between A and T. Many strains of streptococci is present normally in healthy individuals and live in the skin, membranes, and the digestive tract. Streptococci group A can be further categorized into several subtypes based on their M antigen. Generally, streptococci group A are associated with more pathologies and virulence than other streptococcal groups. This is mainly because of the ability of streptococcus group A to invade tissues and cause various diseases like impetigo (invasion of the epidermis), ecthyma (invasion of the dermis), and cellulitis (invasion of deeper layers of the skin) [5].

Infections with streptococcus group A will generally cause edema (in the site of infection), lymphadenopathy, and increased body temperature. Studies have found the presence of the organism in a healthy skin of a child can predict the development of an associated infection within the next ten days. Following colonization of the skin, organisms can move to the oropharynx within the next 1-2 weeks.

Previous large epidemiological studies have concluded that the strains of streptococcus group A organisms that cause impetigo (and other skin infections) are totally different than the strain that cause oropharyngeal conditions. Regardless of this, complications of a streptococcal group infection can include erythema nodosum, rheumatic fever, and acute post-streptococcal glomerulonephritis. Studies

have found that rheumatic fever rarely occurs following a streptococcal skin infection, but glomerulonephritis can sometimes occur following an oropharyngeal streptococcal infection, despite being more common following skin infections.

Unfortunately, even proper treatment of impetigo does not decrease the risk of developing acute glomerulonephritis, but it still does decrease the rates of organism spread to the general population [6]. Glomerulonephritis usually starts to appear within one to three weeks following an oropharyngeal streptococcal infection, but longer following a skin streptococcal infection.

It is rare for beta-hemolytic group A streptococci to cause infections in children younger than 2 years, but its incidence in older ages have been significantly increasing. Currently, it is estimated that up to 5% of children with impetigo will later develop an acute post-streptococcal glomerulonephritis attack [6].

STAPHYLOCOCCI'S CHARACTERISTICS:

One of the important factors in determining virulence of a bacterial organism is its ability to produce superantigens [7]. Superantigens are associated with significant pathology due to their ability to overcome several steps of the normal immune response and therefore induce activation of massive amounts of T cells along with the production of huge amounts of cytokines like interleukin 1, interleukin 6, and tumor necrosis factor α . The result of this will be the development of cutaneous eruptions, severe vomiting, decreased blood pressure, and shock, which may be fatal. Examples of the diseases that are usually caused staphylococcus toxins include impetigo, scalded skin syndrome, and toxic shock syndrome.

Coagulase negative staphylococcus is considered to be the most prevalent organism that inhabits the normal healthy skin. This group contains about eighteen different subtypes with *Staphylococcus epidermidis* being the commonest of them. Coagulase positive staphylococcus aureus can sometimes be temporarily present in the healthy skin, especially in children. Moreover, it can present in the nares of nose of up to one third of the general population, and in the perineum in up to one fifth of the general population.

A previous study has found that more than 60% of patient who developed impetigo were staphylococcal carriers (mostly nasal carriers) [8]. In addition, more than 90% of patients with atopic dermatitis were also

found to be carriers. Many factors have been found to be associated with the development of staphylococcal infections. These include decreased immunity and tissue damage.

IMPETIGO: BULLOUS IMPETIGO

The single most common organism responsible for the development of bullous impetigo is staphylococcus aureus. The most common staphylococcal strain associated with impetigo is group II type 71 [9]. Less commonly, bullous impetigo can be caused by streptococcus group A.

To be able to cause impetigo, staphylococcus aureus needs to secrete the exfoliative toxin that is considered a protease and has the ability to hydrolyze desmoglein-1; an adhesion molecule present intracellularly, selectively. This toxin is considered among the most important factors that make staphylococcus aureus virulent as it leads to the dissociation of cells of the epidermis and leads to the formation of blisters. In patients with impetigo, these blisters are localized, whereas in patients with scalded skin syndrome blisters are generalized. This toxin of staphylococcus aureus has two types: type A which is known to cause bullous impetigo, and type B which is known to cause scalded skin syndrome. Initially, scalded skin syndrome starts following a local conjunctival, nasal, or perioral infection. In rare cases, scalded skin syndrome can occur following staphylococcal pneumonia, arthritis, or endocarditis [10].

The first clinical manifestation of impetigo is the appearance of multiple small vesicles that will soon develop into blisters sized up to 2 centimeters. The content of these blisters is clear at first but will soon become purulent. These blisters usually have a roof that can easily rupture opening to a wet base that has an erythematous shiny color. Remnants of the blister roof can be present in the peripheral parts leading to a polycyclic pattern.

The most common sites where bullous impetigo can occur are the intertriginous areas like the diaper area, the axillary area, and the neck. However, other sites like the palms and the soles can also be affected. Enlargement of regional nodes does not usually occur during the course of impetigo. Finally, it is important to keep in mind that the most commonly affected age by bullous impetigo is 2-5 years [11].

NON-BULLOUS IMPETIGO (CRUSTED):

Up to 70% of impetigo cases are non-bullous. Non-bullous impetigo mainly affects adults but can also

present in children older than two years. It is very rare to occur in infants or children younger than two years old. Both staphylococcus aureus and streptococcus pyogenes are the most common organisms responsible for the development of non-bullous impetigo, with staphylococcus aureus being more common in mid-adulthood, and streptococcus being more common in the elderly. Observational studies from different sites around the world and over the last thirty years have concluded that staphylococcus aureus and streptococcus pyogenes are alone responsible for more than 80% of non-bullous impetigo cases and can be isolated from lesions in most patients [12].

Impetigo can invade both normal skins, or skin affected with different pathologies like atopic/contact dermatitis, bites, scabies, and/or pediculosis. Poor hygienic status and poor nutrition are both associated with the development of impetigo. Lesions are more likely to occur in exposed body sites like the face, the upper limb, and the lower limb. It is relatively common for patients to develop regional lymph nodes enlargements and severe cases may show high fever [13]. Usually, most cases of non-bullous impetigo will spontaneously resolve without any intervention after about 14-21 days of clinical manifestations.

TREATMENT EVOLUTION OF BACTERIAL RESISTANCE:

Unfortunately, staphylococcus aureus, which is the most important cause of impetigo, is associated with high rates of developing resistance against antibiotics, making management and treatment of impetigo challenging.¹⁴ During the last century, almost all strains of staphylococcus aureus have been able to develop resistance against beta-lactam agents (penicillin) leading to inefficacy of treatment. The production of beta-lactamase is considered to be the most common cause of resistance of staphylococcus aureus against antimicrobial treatment.

The emerge of Methicillin-resistant *Staphylococcus aureus* (MRSA) was first noticed in the year 1980. However, the incidence of MRSA infections has been significantly increasing over time. Importantly, the incidence of MRSA infections has been increasing in outpatients, making it an important cause of community acquired infections. However, is still relatively not common for MRSA to develop impetigo in a non-hospitalized individual. When impetigo is associated with furuncles of abscesses, concern for MRSA infection should be present.¹⁵

GENERAL CARE OF PATIENTS WITH IMPETIGO:

When dealing with any patients with impetigo, one of the most important measures is to keep lesions clean, wash them with warm water (with the use of soap), and remove crusts and secretions. Soaps used in the cleaning of impetigo usually contain triclosan, povidone iodine, chlorhexidine, or another antiseptic. However, the efficacy of these antiseptics in impetigo treatment is still debatable with no solid evidence on their efficacy in improving outcomes [16].

INDICATIONS FOR TREATMENT WITH SYSTEMIC ANTIBIOTICS

Most cases can be sufficiently treated with topical antimicrobials; however, systemic treatment may sometimes be needed especially when there is invasion of deep structures like the fascia or the subcutaneous tissues. The presence of high fever, lymph nodes enlargements, associated pharyngitis, or multiple lesions also favor the use of systemic treatment.

SYSTEMIC ANTIBIOTIC THERAPY

The choice of systemic antibiotic for the treatment of impetigo must depend on the cover for streptococci and staphylococci, as both organisms are considered the most common causes of the condition [17]. First choices for treatment include cephalosporins (first-generation) like cephalexin, and penicillin agents that are not sensitive to penicillinase, like cloxacillin and oxacillin.

Erythromycin provides an acceptable option for treatment due to its efficacy against the condition along with relatively cheap price. Erythromycin can also be effective in cases of bacterial resistance against penicillin or cephalosporin. Clarithromycin along with other macrolides are also beneficial and have less rates of adverse events than erythromycin. However, they are more expensive which make them less preferred in many places. Moreover, bacterial resistance against erythromycin means resistance against to other macrolides. In cases of MRSA, antibiotics choices for the treatment of impetigo include tetracycline, sulfamethoxazole / trimethoprim, fluoroquinolones, Clindamycin, and minocycline.

TOPICAL TREATMENT

Strong evidence is present on the superiority of topical antimicrobials for the treatment of local non-complicated cases of impetigo. Moreover, topical antimicrobials treatment is associated with significantly less adverse events than oral systemic

treatment. The best choices of topical treatment against impetigo are fusidic and mupirocin, with both agents having similar efficacy against the disease. On the other hand, the use of neomycin combined with bacitracin has not been found to successfully eradicate the bacteria in impetigo.

FUSIDIC ACID

Fusidic acid has been found by several studies to achieve high efficacy in the eradication of local staphylococcus aureus infections. In addition, it is known to sufficiently penetrate the skin to reach the sites of the infection. Moreover, it has been found to be effective against infections with streptococcus and Propionibacterium. However, it is not effective against infections with gram-negative bacillus organisms.¹⁸ Low rates of bacterial resistance have been associated with fusidic acid. Adverse events following the use of fusidic acid include allergies, which are also not common.

MUPIROCIN

Mupirocin has been studied in several trials and was found to be effective against skin infections with *S. aureus*, and Streptococci. However, it is not effective against gram-negative infections. Interestingly, mupirocin does not kill normal commensal flora making it preferred as it does not lead to alterations in the skin flora. Moreover, bacterial resistance against mupirocin is relatively rare.

About 3% of patients may report the development of adverse events which are mainly allergy, irritation, and itching. Photoreactions can occur but are rare. No systemic adverse events have been observed with mupirocin use as it is not absorbed from the skin, and even when absorbed, it immediately converts into an inactive substance. However, their uses on large areas have been used with nephrotoxicity thus it is only recommended for use in small areas [19].

CONCLUSIONS:

Impetigo is considered to be the most common skin infection that affects children between 2-5 years old. It generally has two types: non-bullous (which is responsible for about 70% of cases) and bullous (which is responsible for the remaining of cases). Non-bullous impetigo can be caused by both staphylococcus aureus and streptococcus pyogenes. It is mainly distinguished by the presence of honey crusts on the face and limbs. Bullous impetigo, on the other hand, is only caused by staphylococcus aureus and results in the development of large bullae and blisters. It generally affects intertriginous body sites.

Most cases of impetigo can resolve spontaneously within few weeks, regardless of the type of impetigo, and the development of late complications is usually rare. However, some cases can be complicated by acute glomerulonephritis, which is sometimes serious. Treatment of impetigo is usually done using either topical or systemic antibiotics. Topical antibiotics are usually preferred in mild non-complicated cases due to their efficacy and safety. On the other hand, systemic treatment is preferred in more severe or complicated cases. Systemic antibiotics is sometimes challenging due the increasing rates of antimicrobial resistance.

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