Review Paper

Investigating COVID-19 Vaccine Coverage Among Iranian Children

Mohammad Sadegh Rezai[1*], Azin Hajialibeig[1], Shaghayegh Rezai[2]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.
2. Department of Medical Microbiology and Virology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

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ABSTRACT

Background: The COVID-19 vaccine could control the COVID-19 crisis worldwide. A total of 85% of the world's population received one dose of the COVID-19 vaccine. One in five children worldwide has currently received zero-dose or under-vaccinated. Meanwhile, 80% of Iranians received at least one dose of the vaccine, and the amount is less in children. Individuals under five years of age have not been vaccinated against COVID-19.

Objectives: This review provides the latest data on COVID-19 vaccinations in children.

Methods: In this review, we searched studies in the following online databases: PubMed, Scopus, Google Scholar, and IranMedex. The search strategy included keywords related to "Vaccine", "COVID-19", "Iran", and "Children" from 2019 to October 2023.

Results: Up to now, there are 242 vaccine candidates worldwide, 822 clinical trials have been conducted for these vaccines, and 50 vaccines have been approved. Also, 12 COVID-19 vaccine candidates were approved in Iran, and 8 vaccines are undergoing clinical trials. Some of these vaccines are allowed to be used for children. Children aged six months to four years should receive three doses of Pfizer-BioNTech or two doses of Moderna from the same manufacturer with at least one dose of the updated vaccine. Mix and match vaccine products are allowed for children above four years of age. The vaccines used in Iran include Covaxin, AstraZeneca, Sputnik V, Sputnik Light, Sinopharm, Barakat Pastovak, Razi Cov Pars, Spicogen Fakhravac, and Noora vaccine. The efficacy of these vaccines is from 65% to 91%. COVID-19 vaccine could be co-administered with other routine or seasonal immunizations. COVID-19 vaccination should be deferred in patients who are symptomatic or asymptomatic COVID-19 infection until the end of their recommended isolation period. The side effects have been similar to other routine vaccines, such as fever, chills, pain in the arm, headache, myalgia, fatigue, redness, and arthralgia. Passive antibody products used to treat COVID-19 illness (higher dose than post-exposure prophylaxis) defer COVID-19 vaccination for 90 days. A tuberculin skin test will not interfere with the response to vaccination. COVID-19 vaccination should not be delayed because of testing for tuberculosis infection.

Conclusions: The vaccination rate of children is lower than that of adults. Also, COVID-19 vaccination can prevent multisystem inflammatory syndrome in children. The planning of COVID-19 vaccination is recommended for children under five years of age in Iran.

Key Words:
COVID-19, Vaccination, Children, Iran

** Corresponding Author:*
Mohammad Sadegh Rezai, Professor.
Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33342334*
E-mail: *drmsrezaii@yahoo.com*

Review Paper

Investigating Rational Usage of Intravenous Immunoglobulin to Treat Multisystem Inflammatory Syndrome in Children

Azin Hajialibeig[1*], Fereshteh Rostami-Maskopaee[2]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.
2. Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Multisystem inflammatory syndrome in children (MIS-C) is a presentation of coronavirus infection 2019 (COVID-19). MIS-C is uncommon but can lead to life-threatening illnesses. Some MIS-C patients had Kawasaki disease symptoms, including mucocutaneous involvement, conjunctivitis, lymphadenopathy, and elevation of inflammatory markers. According to the Center for Disease Control checklist, the diagnostic criteria of the MIS-C checklist included the following items: Fever lasting for at least 24 h, laboratory evidence of inflammation without any other cause and involving at least two organs, and proof of SARS-CoV-2 infection. Initial treatment depends on the severity of the illness; meanwhile, clinical findings include fluid resuscitation, inotropic support, and respiratory support, immunomodulatory therapies (intravenous immunoglobulin [IVIG], glucocorticoids, and anakinra). Until now, there has been a lack of evidence-based guidelines to treat MIS-C patients.

Objectives: We performed a literature review on the rational usage of IVIG for managing MIS-C patients. The use of IVIG as a treatment was based on the similarities with Kawasaki disease.

Methods: We have searched in the Pubmed and Scopus databases for full texts in English and Persian with the following keywords: MIS-C, IVIG, and glucocorticoids.

Results: Our review yielded 427 studies. Of these studies, eight articles were included in this review. All patients had fever at the time of admission, and the most common comorbidity in studies was obesity. The most clinical manifestations of MIS-C patients were gastrointestinal and respiratory. The clinical outcomes, including death, need for an intensive care unit, and need for a ventilator in MIS-C patients treated with IVIG alone were better than those in the IVIG with corticosteroids (CS) group. Therefore, it is reasonable to provide IVIG. We should be cautious in interpreting the study's results because the disease's severity was not mentioned in all studies, and all studies were observational. One of the latest approaches suggests the concomitant administration of IVIG and glucocorticoid can be given in coronary artery involvement and or critically ill patients.

Conclusions: There is limited evidence to support the use of IVIG only or IVIG with CS. The best studies for the effective role of drugs are randomized clinical trial studies. Further studies with double-blind clinical trial designs are needed to determine the best treatment for managing MIS-C patients. Also, a systematic review and meta-analysis study is suggested to compare the use of IVIG only or IVIG with CS.

Key Words:
Intravenous immunoglobulin (IVIG), Multisystem inflammatory syndrome, Children

** Corresponding Author:*
Azin Hajialibeig, Assistant Professor.
Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33342334*
E-mail: *azin.hajialibeyg@gmail.com*

Review Paper

Investigating Acute Rheumatic Fever, Dilemma, and Challenges

Leila Shahbaznejad[1*]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Acute rheumatic fever (ARF) is still a health problem in developing countries. The consequence of beta-hemolytic group A *streptococcus* pharyngitis in a susceptible host can be complicated with ARF. Rheumatic heart disease is the chronic sequel of ARF and has been accompanied by cardiac-related mortality in young people. In 1944, Duckett Jones described the criteria for diagnosis of the disease. These criteria were revised in 1992 and 2015 by the American Heart Association. The five primary criteria are carditis, arthritis, chorea, erythema marginatum, and subcutaneous nodules. Minor criteria are fever, arthralgia, prolonged PR interval on electrocardiogram, increased erythrocyte sedimentation rate, or CRP. Hence, this set of criteria was helpful in the management of the disease. Diagnosing the diseases is not easily possible, especially in milder or missed cases. In 2015, the American Heart Association revised the criteria depending on the susceptibility of the societies to ARF; therefore, the threshold of the criteria for definition of the patients in moderate to high prevalence population changed to lower levels, and patients with more atypical presentation or milder complications could be diagnosed with ARF. These changes resulted from monoarthritis or poly arthralgia, the lower cut-off for fever, and erythrocyte sedimentation rate. Another important aspect of this revision is the necessity of echocardiography for suspected or confirmed cases of ARF instead of only clinical carditis; accordingly, subclinical valvular regurgitation could be genuinely diagnosed. On the other hand, just auscultatory murmur with normal echocardiography could rule out cardiac involvement. In this condition, the quality of clinical auscultatory skills and other physiologic or pathologic murmurs could be distinguished well by cardiac echocardiography. In the recent guideline, valvular involvement characteristics during ARF were described to differentiate rheumatismal heart disease from other valvular diseases. Chemoprophylaxis is the mainstay of breaking the cycle of ARF, from acute pharyngitis to rheumatic heart disease. Penicillin is still effective against streptococcal pharyngitis and can maintain good plasma levels for at least four weeks in benzathine preparation. Although other antibiotics may be effective, they have not been advised for ARF prophylaxis because of their short half-life and multiple daily doses. Depending on the severity of heart damage, the duration of prophylaxis may be from 5 to 10 years or until 21 years of age, whichever is longer. In some patients who suffer from severe valvular complications, lifelong prophylaxis is recommended. Despite global advantages in understanding and diagnosis of ARF, it is predictable that a considerable amount of missed cases of ARF and rheumatic heart disease remain undiagnosed in developing countries. A guideline or approach for case finding or management of this health issue is greatly needed.

Key Words:

Acute rheumatic fever (ARF), Rheumatic heart disease

** Corresponding Author:*
Leila Shahbaznejad, Assistant Professor.
Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33342334*
E-mail: *leilashahbaznezhad@gmail.com*

Review Paper

Investigating Measles Resurgence: An Overview

Mohammad Jafar Saffar[1*]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Fifty years after the introduction of measles vaccination, the epidemiology of measles changed markedly, and the incidence of reported measles cases and related deaths declined significantly. However, measles cases and deaths have increased steadily globally in recent years. The main reasons for this resurgence, as well as the most appropriate policies to reduce the number of cases and control the resurgence, are reviewed in this article.

Objectives: The main reasons for this resurgence, as well as the most appropriate policies to reduce the number of cases and control the resurgence, are reviewed in this article.

Methods: The number of measles cases reported to the World Health Organization (WHO) per year in each country, and the leading causes of the outbreaks were analyzed.

Results: This review showed that inadequate vaccination rates were the leading cause for the resurgence; however, many factors, such as personal, philosophical, religious, or concerns about the vaccine's safety, along with lack of access to vaccines, were also responsible.

Conclusions: This study showed that measles vaccination rates increased steadily from 2000 to 2011 and plateaued in 2018 as follows: For Mv1, from 72% to 86%, and for Mv2, from 17% to 74%. Accordingly, the number of reported measles cases decreased substantially globally to 132 490 cases in 2016 (the lowest recorded cases since vaccination). However, due to inadequate measles vaccination rates capable of preventing or controlling the spread of infection, the number of reported cases began to increase worldwide in 2018 and reached 869 770 cases in 2019. Many countries have experienced large outbreaks, and some countries have lost their measles elimination status. Many factors with different effects between countries were found to be responsible for inappropriate vaccination levels. The most critical factors were as follows: Personal or physiological beliefs, religious concerns about the safety of vaccines, and the lack of access to vaccines. One of the most common explanations is a set of beliefs promoting reluctance to take childhood vaccination that was labeled as vaccine hesitancy by the WHO and the most severe threat to public health. The COVID-19 pandemic had significant adverse effects on children's vaccination worldwide. Over 60 million doses of measles vaccine were postponed or missed. This increased the risk of more significant outbreaks worldwide. After the pandemic, measles cases worldwide rose by 79% in 2022, a worrying sign of an increased risk of more extensive outbreaks. There are multiple challenges to achieving and maintaining the measles herd immunity threshold (nearly 95%). Strategies to prevent and control measles are as follows: Achieving and maintaining high levels of population immunity >95% for first and second doses of measles vaccine and targeted supplementary immunization activities.

Conducting high-quality case-based surveillance and periodic monitoring of immunity to identify immunity gaps and guide targeted supplementary immunization is recommended to maintain herd immunity and prevent outbreaks.

Key Words:

Measles, Epidemiology, children's vaccination, Immunity gaps

** Corresponding Author:*

Mohammad Jafar Saffar, Professor.

Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*

Tel: *+98 (11) 33342334*

E-mail: *saffar@softhome.net*

Research Paper

Investigating Ferritin Thresholds for Cardiac and Liver Hemosiderosis in β-thalassemia Patients

Mohammad Naderisorki[1*], Hadi Darvishi-Khezri[1], Aily Aliasgharian[1], Hossein Karami[1], Hanie Fallah[1], Mobin Ghazaiean[1]

1. Thalassemia Research Center, Hemoglobinopathy Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Signs of iron overload are among the most common clinical concerns related to β-thalassemia patients. In these cases, the ferritin test is frequently used as an alternative method for magnetic resonance imaging.

Objectives: The current study introduces the best cutoff points for liver and cardiac hemosiderosis in patients with β-thalassemia.

Methods: This was a retrospective diagnostic study of registered data of β-thalassemia patients (n=1959) in Mazandaran Province, Iran. T2*-weighted magnetic resonance imaging was considered a reference test for liver and cardiac hemosiderosis. The index test (ferritin levels) was gauged through a chemiluminescent immunoassay.

Results: At a cutoff point of 2027 ng/mL, ferritin levels had a sensitivity of 50%, specificity of 77.4%, positive predictive value of 42.1%, and negative predictive value of 82.5% for cardiac hemosiderosis (area under curve=0.66, 95% CI, 0.60%, 0.71%, adjusted odds ratio=2.05, 95% CI, 1.05%, 4.01%). With a cutoff point of 1090 ng/ mL, the ferritin test demonstrated a sensitivity of 66.7%, specificity of 68%, positive predictive value of 82.9%, and negative predictive value of 46.8% for liver hemosiderosis (area under cover=0.68, 95% CI, 0.63%, 0.73%, adjusted odds ratio=3.93, 95% CI, 2.02%, 7.64%).

Conclusions: Optimum cutoff points of the ferritin test to screen cardiac hemosiderosis indicated a comparatively feeble sensitivity and specificity. The probability of cardiac hemosiderosis at a 2027 ng/mL cutoff point for ferritin was equal to 17.5%. Regardless of the siderosis severity, ferritin levels above 1090 ng/mL might predict 82.9% of β-thalassemia patients with liver hemosiderosis. Our findings suggest that the ferritin test would be more deserving for screening for liver hemosiderosis than cardiac hemosiderosis in β-thalassemia patients.

Key Words:

β-thalassemia, Cardiac hemosiderosis, Ferritin

** Corresponding Author:*
Mohammad Naderisorki, Assistant Professor.
Address: *Thalassemia Research Center, Hemoglobinopathy Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33347837*
E-mail: *dr.naderisorki@gmail.com*

Review Paper

Investigating the Effects of Presurgical Orthopedics on Facial Aesthetics in Infants With Cleft Lip and Palate

Parastoo Namdar[1*]

1. Dental Research Center, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Cleft lip and palate are the most frequent congenital pathology of the maxillofacial territory. They correspond to a malformation consisting of a lack of fusion of the corresponding embryological processes, whether the lip, palate, or both. They have a multifactorial etiology, with genetics and environment playing an important role. These disorders cause morphological and functional alterations in the masticatory, aesthetics, phonatory, auditory, and respiratory functions.

Methods: Different approaches are suggested to achieve an orthopedic effect. The approach selection is usually determined by the operator's preference and the type of cleft to be treated. The maxillary segments of the child with a bony cleft are molding and repositioning if suitable appliances are used in the neonatal period. The ultimate goal is to attain an end-to-end position of the alveolar processes before lip operation. A combination of intra-oral appliances and extra-oral orthopedic strapping can be used in preparation for primary lip and palate surgery. Elastic forces will exert a retracting, backward pressure against the protruding pre-maxilla, and careful use of forces on the cleft segments will improve their positions and allow definitive lip skin and muscle repair. In this approach, a nasal stent is attached to the intra-oral mouth plate and is designed to improve nasolabial anatomy.

Results: Individuals with cleft lip and palate should be evaluated very carefully. Enough knowledge regarding malocclusion and long-term orthodontic intervention is needed to manage patients with cleft lip and palate successfully. Advances in correcting deformity by team approach in cleft lip and palate management allow for markedly increasing success levels. The functional and esthetic improvement achieved in these patients has already reached a level that ensures optimum adaptation to the social environment and comfort of these patients. The advantages of presurgical orthopedics include psychosocial relief of the infant's family. Preliminary findings indicate that the frequent visits for nasoalveolar molding adjustments reduce the anxiety felt by the caregiver and lead to a sense of empowerment. Presurgical orthopedic also reduces the overall cost of cleft care by reducing the number of subsequent nasal revisions, allows for gingivoperiosteoplasty during initial lip repair in over 90% of infants, and eradicates secondary alveolar bone grafts in over 60% of patients. The combined benefits of enhanced nasal symmetry and appearance and decreased number of nasal and dentoalveolar procedures result in considerable financial savings and the patient's and family's psychological well-being. Furthermore, no effect on the growth of the midface in the sagittal and vertical plane has been recorded up to the age of 18 years in patients who have undergone this procedure.

Conclusions: Presurgical orthopedics can reduce alveolar cleft width and lip width relative to the growth of the face. Moreover, tension will be reduced with minimal risk for scar formation when the distance between gingival tissues is closed or reduced to a minimal level. Accordingly, correction of deformity at the lip, nose, and alveolar region can be treated by a single surgery.

Key Words:
Presurgical orthopedics, maxillofacial, Cleft lip and palate, Alveolar region

** Corresponding Author:*
Parastoo Namdar, Assistant Professor.
Address: *Dental Research Center, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33543852*
E-mail: *namdarp881@mums.ac.ir*

Case Report

Examining the Airway Obstruction: A Pediatric Case Report

Mohammad Reza Navaeifar[1*]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Opening the airways is a prerequisite for normal breathing. In the initial approach to every critical patient, it is necessary to ensure the airway is open in the first step. The airways in children are different from those in adults and require more attention.

Objectives: This report reports a case of upper airway obstruction due to burns.

Methods: A 16-month-old child accidentally swallowed an unknown amount of boiling water and subsequently suffered burns to their throat and mouth. The steps of approach to this patient and the final fate of the patient are reported in this article.

Results: This child was taken to a local clinic a few minutes after the burn. In the clinic, after the examination, it was recommended to go to the burn center, which was about 90 min away. The patient was taken to the burn center by private vehicle. At the time of presentation, the patient had mild drooling and stridor. Outpatient treatment was given with intravenous fluids in addition to ampoules of dexamethasone and hydrocortisone. After the initial treatment at the burn center, the patient was referred to the otolaryngology referral center in about 30 min to continue the treatment on an outpatient basis. The patient was pale, confused, and restless when entering the final center. Oxygen saturation was 88%, and blood pressure was reported at 100/55 mm Hg. He had severe stridor and drooling. The supine position aggravated the patient's hypoxemia and restlessness. The oral mucosa and tongue were erythematous and swollen. Minutes after entering and during initial evaluations and administration of oxygen, the patient had a sudden cardiac arrest and cyanosis. The cardiopulmonary resuscitation was started, and 5 min later, while the patient was being resuscitated, tracheal intubation was performed with an uncuffed tracheal tube size 3.5 French. During laryngoscopy, the aryepiglottic folds were edematous and erythematous, and the vocal cords were slightly swollen. Despite advanced cardiopulmonary resuscitation, the patient died after 40 min. The challenges that occurred in this case, which could have been avoided, ultimately caused the death of the patient. In summary, insufficient attention to the symptoms of airway obstruction, inappropriate handling of a child who had symptoms of airway obstruction, unsafe patient transfer, and inadequate attention to quick and proactive airway management in a child were the most critical challenges of this case.

Conclusions: Airway obstruction is one of the vital emergencies that cannot be ignored in critically ill patients, especially children. It is essential to pay close attention to any signs of airway obstruction and to be evaluated and treated immediately. Carefulness in scientific, ethical, and legal aspects is necessary to prevent further complications.

Key Words:

Children, Burn, Airway

** Corresponding Author:*

Mohammad Reza Navaeifar, Assistant Professor.

Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*

Tel: *+98 (11) 33342334*

E-mail: *dr.navaifar@gmail.com*

Review Paper

Investigating the Frequency of Bacille Calmette Guerin Vaccine Complications in Iran

Fatemeh Varshoei[1*], Fereshteh Rostami-Maskopaee[2]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.
2. Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: The Bacille Calmette Guerin (BCG) vaccine is part of some countries' global expansion programs for vaccination. One dose of vaccine is recommended at birth. Although the BCG vaccine has not been used to prevent the disease, it reduces the incidence of severe forms, including meningitis and miliary tuberculosis. BCG vaccine may cause some complications, including cellulitis and abscesses at the injection site, lymphadenitis, BCGosis, hepatosplenomegaly, rash, and weight loss. Regarding previous studies, lymphadenitis is among the most common complications reported in about 2% of subjects. Complication rates significantly increased with T-cell defects, such as severe combined immunodeficiency (SCID), Mendelian susceptibility to mycobacterial disease, chronic granulomatous disease, and HIV. Based on the available documentation, there is little information about the incidence of BCG vaccine side effects in Iran.

Objectives: This study focuses on the frequency of BCG vaccine side effects in Iran.

Methods: In the present systematic review, we performed electronic searches in the following databases: Web of Science, PubMed, Scopus (1990 to September 2023), and Google Scholar. The selected keywords related to BCG vaccination and BCG vaccination complications were also used for the search. Relevant studies with BCG vaccine-related complications were included.

Results: Although BCG vaccines are considered highly safe in immune-competent hosts, complications can occur. Different studies have shown that the complications of BCG vaccination appear within six months after birth. Lymphadenitis is one of the most common complications. Some studies showed that the incidence of disseminated BCG infection is more common in boys compared to girls. The most common complications are lymphadenopathy and lymphadenitis. The most common lymph node involved is the axillary lymph node. Complications of BCG vaccination can be severe and life-threatening in infants with immunodeficiency. SCID is the most severe form of primary immunodeficiency disease, and BCGosis as a side-effect of the BCG vaccine could be seen in all underlying genetic types of SCID.

Conclusions: Severely immunocompromised infants are at the highest risk of BCGosis and do not respond well to standard therapies. To avoid severe BCG complications, screening for PIDs should be performed before BCG inoculation for individuals with positive family histories of PIDs.

Key Words:
Bacille Calmette Guerin, Adenitis, BCGosis, Primary immunodeficiency diseases

** Corresponding Author:*
Fatemeh Varshoei, Assistant Professor.
Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33342334*
E-mail: *mehranav2012@yahoo.com*

Review Paper

Examining the Comprehensive Child Sexual Education: A Review of Content and Outcomes

Soghra Khani[1*], **Zahra Barimani Aboksari**[1]

1. Sexual and Reproductive Health Research Center, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Sexuality encompasses vast areas, including sex, gender identity, gender roles, sexual orientation, pleasure, intimacy, and reproduction. Child sexual education will help them make better decisions regarding sexual health and prevent the specific problems they face.

Methods: In this review, online databases, including Google Scholar, Web of Science, Science Direct, Scopus, and PubMed, were searched to retrieve articles published up to November 2023 using the following keywords: Child, sexual health, sexual education, and outcome. A total of 97 studies that were related to the topic were extracted. After title and abstract screening, 57 articles were and then in full-text screening, 26 articles were excluded. Finally, 14 articles were used to write this review.

Results: Comprehensive child sexual education included the following topics: Relationships, values, rights, culture, sexuality, understanding gender, violence and staying safe, skills for health and Wellbeing, the human body and development, sexuality and sexual behavior, and sexual and reproductive health. The consequences of sex education for children were the improvement in the following areas: Sex-related knowledge and attitudes, such as inappropriate touch, self-protective behaviors, girls, body esteem, and protective changes on HIV/AIDS knowledge, sexual perceptions, condom use intention, youth's sexual abstinence/protected sex, parent-child communication about sex and decreases in teen pregnancy, and gender typing of others among girls.

Conclusions: Child sexual education can guarantee the sexual health of the coming years of life; therefore, it is necessary to plan and make policies to institutionalize this training in society.

Key Words:
Child, Sexual health, Review

** Corresponding Author:*
Soghra Khani, Associate Professor.
Address: *Sexual and Reproductive Health Research Center, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33367344*
E-mail: *s.khani@mazums.ac.ir, khanisog343@gmail.com*

Review Paper

Examining the Emergence of Carbapenem-resistant Gram-negative Nosocomial Infections in Children

Golnar Rahimzadeh[1*], Mohammad Sadegh Rezai[1]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: The rise of extended-spectrum β-lactamases strains since 2000 led to a surge in the use of carbapenems in clinical settings. This has also increased the number of clinical bacterial isolates producing carbapenemases. Carbapenem-resistant organisms (CRO) can resist carbapenems in different ways. There are three ways that CRO can resist carbapenems: Porin-mediated resistance, efflux pumps, and carbapenemases-mediated resistance. Carbapenemases are classified into three categories as follows: Class A, class B, and class D enzymes. As a healthcare professional, it is essential to be aware of the increasing prevalence of resistance to carbapenems and stay current to provide the best possible care for our patients.

Methods: Our review involved a comprehensive search of studies indexed in multiple international databases, including PubMed, Web of Science, Scopus, and Google Scholar. We specifically looked at studies published from 2012 to 2023 with the following MeSH terms: "Gram-negative bacterial", "carbapenems", "carbapenem-resistant", and "children".

Results: Our literature search yielded 8600 studies, and 63 English-eligible articles were included in our analysis. Based on the findings, the highest colonization of CRO occurred in cases of blood infections. The most common resistance mechanism in CRO was carbapenemase production due to the presence of genes located on transposable elements and easily transferred between bacteria. The prevalence of resistance to imipenem and meropenem were 81.1% and 83.6%, respectively; however, doripenem is highly stable against hydrolysis, and it also boasts lower minimum inhibitory concentrations than both meropenem and imipenem. *OXA-23*, *OXA-24*, and *OXA-58* genes were quite prevalent among class D carbapenemases, with a rate of 73.7%, 21.9%, and 6.2%, respectively. Additionally, among class B carbapenemases, the prevalence of *IMP*, *VIM*, and *NDM* genes was 16.7%, 12.3%, and 2.7%, respectively. Also, during the COVID-19 pandemic, an increase in the frequency of *NDM*, *KPC*, *OXA-48*, and *VIM* genes was reported. Studies showed CRO rates as high as 45% for *Klebsiella pneumonia*, 38% for *Pseudomonas aeruginosa*, and 36% for *Enterobacter* spp in pediatric intensive care units and oncology wards. The CRO rates are also alarming in neonatal intensive care units for *Acinetobacter baumannii*, *P. aeruginosa*, *K. pneumonia*, *Enterobacter* spp., and *Escherichia coli* had rates of 78%, 31%, 35%, 20%, and 15%, respectively. The mortality has been found that rate among children who received meropenem and imipenem for an infection caused by CRO with a minimum inhibitory concentration of >8 mg/L was higher compared to those who received meropenem with a minimum inhibitory concentration of ≤8 mg/L. All children infected with CRO with meropenem MICs of ≥32 mg/L died.

Conclusions: Considering the increasing prevalence of resistance to carbapenems, especially during the COVID-19 pandemic, it is advised to avoid prescribing carbapenems as the first line for empirical treatment of infections caused by CRO strains. For treatment of infections caused by CRO, combinations of β-lactams and β-lactamase inhibitors, such as piperacillin/tazobactam, ceftazidime/avibactam, meropenem/tazobactam, imipenem/cilastatin/sulbactam, and ceftolozane/tazobactam are suggested.

Key Words:

Carbapenem-resistant,
Gram-negative,
Nosocomial infections,
Children

** Corresponding Author:*

Golnar Rahimzadeh, Assistant Professor.

Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*

Tel: *+98 (11) 33342334*

E-mail: *rahimzadehgolnar@yahoo.com*

Review Paper

Investigating the Effects of Probiotics, Prebiotics, and Symbiotics in Pediatric Infectious Diseases

Shaghayegh Rezai[1*], Raha Rezai[2], Saman Soleimanpour[1]

1. Department of Medical Microbiology and Virology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran:
2. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Probiotics, prebiotics, and symbiotics have gained significant attention in infectious diseases due to their potential to prevent and manage various infections. Studies have been performed on these products concerning acute gastroenteritis, respiratory tract infections, and urinary tract infections. Modulating the intestinal microbiota plays a vital role in the functioning of the immune system and preventing infectious diseases in children.

Objectives: The purpose of this study was to review the medical uses of probiotics, prebiotics, and symbiotics in pediatric infectious diseases and summarize the current understanding of their potential health advantages.

Methods: Our review applied a comprehensive literature search of studies indexed in multiple international databases, including PubMed, Scopus, and Google Scholar. Randomized controlled trials, meta-analyses, and observational studies were included. We specifically looked at studies published from 2012 to 2023 with the following keywords: "Probiotics", "prebiotics", "symbiotics", and "pediatric infectious disease".

Results: Our literature search yielded 8935 reviews and 51 articles included in our analysis. In pediatric infectious diseases, probiotics, prebiotics, and symbiotics have shown promise in preventing and managing various infections. These products have shown promising effects on the outcome of pediatric cystic fibrosis. Evidence indicated that administering *Laciticaseibacillus rhamnosus*, *Limosilactobacillus reuteri*, and *Lactiplantibacillus plantarum* through fecal inoculation daily for 20 days can enhance lung function, decrease pulmonary exacerbation, and improve the nutritional status of children with cystic fibrosis. Probiotic intervention has been explored in gastrointestinal diseases, such as inflammatory bowel disease, irritable bowel syndrome, acute gastroenteritis, and antibiotic-associated diarrhea. Oral administration of *L. rhamnosus* and *Saccharomyces* for 5 to 14 days has been confirmed to reduce disease activity, alleviate symptoms, and enhance bowel health in children. These probiotics impact various aspects of gastrointestinal function, including the barrier function of the gut, innate immunity, autophagy, adaptive immunity, metabolism, and cellular homeostasis. Furthermore, using probiotics in immune-compromised children was controversial in different studies.

Conclusions: Probiotic consumption holds promise in managing pediatric gastrointestinal diseases, cystic fibrosis, and antibiotic-associated diarrhea; however, further research is needed to determine optimal strains, doses, and treatment durations. Probiotics have the potential to offer safe and effective adjunctive therapies for these conditions. Still, healthcare professionals should consider individual patient characteristics and consult guidelines for appropriate probiotic use in pediatric populations.

Key Words:
Probiotics, Prebiotics, Pediatrics, Infectious diseases

** Corresponding Author:*
Shaghayegh Rezai
Address: *Department of Medical Microbiology and Virology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran:*
Tel: *+98 (911) 3289403*
E-mail: *rezai.shaghayegh1992@gmail.com*

Research Paper

Comparing the Effects of Internet-based Cognitive Behavioral Therapy and Art Therapy on Children With Generalized Anxiety Disorder: A Randomized Double-blind Clinical Trial

Samaneh Farnia[1*], Seyedeh Samineh Fattahi[1], Ladan Foladi[1], Seyedeh Farzaneh Fattahi[2], Mahsa Tashakori[1], Leila Arab[3], Maryam Ghorbani[4]

1. Psychiatry and Behavioral Sciences Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran.
2. Girls Technical and Vocational University, Sari, Iran.
3. Department of Educational Psychology, Faculty of Psychology and Educational Sciences, Adib University, Sari, Iran.
4. Department of Counseling, Faculty of Psychology and Educational Sciences, Allameh Tabatabai University, Tehran, Iran.

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ABSTRACT

Background: Generalized anxiety disorder (GAD) is one of the most common childhood psychiatric disorders that continues into adulthood if untreated. Despite the high prevalence of these disorders, they are not diagnosed and treated correctly in 80% of cases.

Objectives: This study compares the effect of internet-based cognitive behavioral therapy (ICBT) and art therapy with the drawing approach on GAD in children.

Methods: This randomized clinical trial was conducted on children aged 8 to 10 with GAD referred to the Educational Clinic of Mazandaran University of Medical Sciences in 2022. The participants were selected from eligible children on the waiting list. The evaluation was done with Kiddie schedule for affective disorders and schizophrenia- present and lifetime version, strength and difficulties questionnaire, and Spence children's anxiety scale. The block randomization method allocated the participants into three groups of 15 children. The first group received eight sessions of art therapy. The second group received eight sessions of ICBT. The third group (control) received only supportive services. The evaluations were done before the first session, immediately after the end of the intervention, and two months later (follow-up). Data analysis was performed using the SPSS software, version 20.

Results: There were no statistically significant differences between the three groups regarding demographic and essential variables at the beginning of the study. Repeated measures analysis of variance showed that in the ICBT group, the mean anxiety score immediately after the intervention and at the follow-up time had a significant decrease compared to before the intervention (P=0.0009). The art therapy group obtained the same results (P=0.0009). The mean anxiety score changes during the study in the ICBT group were higher than the control group (P<0.000). The mean changes in anxiety score in the ICBT group were also higher compared to the art therapy group (P=0.0003). There was no significant difference between the art therapy group and the control group in terms of changes in anxiety scores (P=0.322).

Conclusions: ICBT is more effective compared to art therapy in reducing the anxiety scores of children with GAD.

Key Words:
Internet-based cognitive behavioral therapy (ICBT), Art therapy, Generalized anxiety disorder, Children

** Corresponding Author:*
Samaneh Farnia, MD.
Address: *Psychiatry and Behavioral Sciences Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33273024*
E-mail: *sm.farnia@gmail.com*

Review Paper

Investigating Congenital Cardiac Complications in Infants Born to Mothers Treated With Venlafaxine

Mahsa Kamali[1], Marzieh Azizi[2], Forouzan Elyasi[2*]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.
2. Sexual and Reproductive Health Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Congenital heart complications have a high therapeutic and care pressure on newborns. In some cases, these side effects occur following drug use during pregnancy. According to the results of a study in Iran, the prevalence of depression in pregnant women was reported as 41.22%. In a study, the prevalence of congenital heart disease in babies whose mothers were treated with antidepressants during pregnancy was 18%.

Objectives: Considering the increasing use of venlafaxine in the hospital, this study reviews congenital heart complications in babies born to mothers treated with venlafaxine.

Methods: The present review study was conducted on November 3 and 4, 2023, independently by two researchers in Google Scholar, PubMed, PsycINFO, Web of Science, Cochrane Library, and Science Direct databases without time limitation. The search strategy was based on the MeSH keywords as follows: "Venlafaxine" OR "effexor" OR "SNRI" AND "pregnancy" OR "pregnant women" AND "congenital heart anomalies" OR "congenital cardiac anomalies" OR "septal defect". All articles in Persian and English were included in the study. Review studies were excluded from the present study. Finally, four studies that did not have high quality based on the Newcastle-Ottawa scale tool were reviewed.

Results: In the present study, one prospective cohort study and three case-control studies were investigated. The results of the studies showed that the use of venlafaxine during pregnancy to manage depression would lead to congenital heart defects with a frequency of 14.5% and an odds ratio of 1.23. Also, atrial and ventricular wall defects with a frequency of 9.1% and an odds ratio of 1.17 were reported. In addition, the results of another study showed that the frequency of congenital heart defects in babies whose mothers used venlafaxine in the first trimester was not significantly different (1.5% vs 1.2%). The findings of another study showed that the rate of congenital heart defects in babies born to mothers treated with venlafaxine was 1.15%.

Conclusions: The results of the present review study showed limited evidence for the safe administration of venlafaxine during pregnancy for the management of depression in pregnant women. Considering the severe and dangerous consequence of congenital cardiac anomaly in infants, it is suggested that health professionals should consider precautions for the safe administration of venlafaxine.

Key Words:

Venlafaxine, Ventricular Septal defect, Congenital malformation, Antidepressant, Pregnancy

** Corresponding Author:*
Forouzan Elyasi, Professor.
Address: *Sexual and Reproductive Health Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (911) 1551097*
E-mail: *forouzan.elyasi@gmail.com*

Research Paper

Investigating the Two Independent Risk Factors for Vitamin D Insufficiency of Patients With β-thalassemia: Raised Aspartate Aminotransferase and Moderate to Severe Liver Siderosis

Hossein Jalali[1*], Hossein Karami[1], Hadi Darvishi-Khezri[1], Mohammad Zahedi[1], Mehrnoush Kosaryan[1], Mobin Ghazaiean[1]

1. Thalassemia Research Center (TRC), Hemoglobinopathy Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: One of the side effects of chronic blood transfusion in β-thalassemia patients is vitamin D (Vit-D) deficiency.

Objectives: The current study investigates the Vit-D status and its risk factors in β-thalassemia patients.

Methods: This was a multicenter and observational study covering all β-thalassemia patients from Mazandaran Province, Iran. The study population included transfusion-dependent and non-transfusion-dependent thalassemia patients who belonged to 14 hospital-based thalassemia sections or clinics from December 2015 until December 2019. Demographic data, clinical findings, and some biological tests besides T2*-weighted magnetic resonance imaging were considered for analysis. Meanwhile, 25(OH)D3 levels (ng/mL) have been gauged through high-performance liquid chromatography.

Results: Among 1959 registered data, the serum levels of Vit-D were available for 487 (24.9%) patients. The prevalence of Vit-D insufficiency (<30 ng/mL) was 41.9, with a 95% confidence interval of 37.5-46.3. The adjusted risks of increased aspartate aminotransferase and moderate to severe liver siderosis for Vit-D insufficiency (<30 ng/mL) were estimated at 2.62, with a 95% confidence interval at 1.43-4.79 and 2.31 with 95% confidence interval at 1.38-3.89. According to the receiver operating characteristic curve analysis, the accuracy of ferritin levels with a cutoff point of 1078 ng/mL for prediction of Vit-D insufficiency condition was equal to 0.61 with 95% confidence interval at 0.54 - 0.68 (P=0.03, sensitivity=67%, specificity=49%, positive predictive value=47%, and negative predictive value=68%).

Conclusions: Despite efforts for supplement prescriptions related to the national programs for treating Vit-D deficiency in all patients, our patients also have Vit-D insufficiency. We demonstrated that increased aspartate aminotransferase and moderate to severe liver siderosis were identified as the independent risk factors for Vit-D insufficiency in patients with β-thalassemia.

Key Words:

β-thalassemia, Vitamin D insufficiency, Risk factor

** Corresponding Author:*

Hossein Jalali, Assistant professor

Address: *Thalassemia Research Center (TRC), Hemoglobinopathy Institute, Mazandaran University of Medical Sciences, Sari, Iran.*

Tel: *+98 (11) 33347837*

E-mail: *jalali@khu.ac.ir*

Research Paper

Investigating Multisystem Inflammatory Syndrome in Children Outcomes in Obesity Patients Referring to Boo-Ali Sina Hospital in Sari City and Shafizadeh Hospital in Babol City, Iran

Fereshteh Rostami-Maskopaee[1], Faezeh Sadat Movahedi[2], Mohammad Sadegh Rezai[2*]

1. Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.
2. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Multisystem inflammatory syndrome in children (MIS-C) is one of the multi-system inflammatory diseases following COVID-19, which has been observed in children with the involvement of at least two organs, and if not diagnosed and treated, it can be a life-threatening illness. Numerous studies have been published internationally that obesity is a major risk factor for adverse outcomes in the COVID-19 pandemic.

Objectives: Considering the significant role of obesity in the severity of COVID-19, this study investigates the MIS-C outcomes in overweight and obese patients referring to Boo-Ali Sina Hospital in Sari and Shafizadeh Hospital in Babol City, Iran.

Methods: In this cross-sectional study, all MIS-C patients over 21 years of age from December 2019 to September 2023 were studied. The Centers for Disease Control and Prevention checklist identified the patients. Overweight and obese children were calculated according to the World Health Organization (WHO) definition based on the age and sex of each child. The outcomes included pediatric intensive care unit admission, hospitalization, the need for a ventilator, and death. The data were analyzed using the t-test, along with Mann-Whitney, and chi-square tests in the SPSS software, version 16.

Results: The total number of MIS-C patients referred to two hospitals was 174. The height and weight information was available for 149 patients. The median age was 62 months (27-92 months). A total of 65% were boys, and all had a fever at the time of admission. Gastrointestinal symptoms were the most common symptoms in both groups. Intensive care unit admission in the obese and without obese groups was 60.47% and 22.64%, respectively. Death in the obese group was 2.33%, and in the non-obese group was 0.94%. Also, the median hospital stay in the obese group was 9 days (7-13), and in the non-obese group was 8 days (6-10). There were significant differences between the two groups in hospital stay, pediatric intensive care unit admission, intensive care unit stay, cardiac symptoms, and comorbidity (P<0.05).

Conclusions: According to the results of the study, obese MIS-C patients have more severe courses and outcomes; therefore, early attention at the time of admission in this group is necessary.

Key Words:
Multisystem inflammatory syndrome in children (MIS-C), Obesity, Children

** Corresponding Author:*
Mohammad Sadegh Rezai, Professor.
Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33342334*
E-mail: *drmsrezaii@yahoo.com*

Review Paper

Investigating the Effects of Multiple Wavelength Irradiance of Phototherapy on Biochemical Alteration in Jaundiced Neonates: A Review

Roya Farhadi[1*], Seyed Amir Kazemi[2]

1. Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.
2. Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Phototherapy is a standard treatment for neonatal hyperbilirubinemia. Light absorption by the skin transforms bilirubin from non-polar Z, Z- to polar isomers of bilirubin: Configurational isomers of Z, E- and E, Z-bilirubin and structural isomers of E, Z- and E, E-lumirubin. These photoisomers can be excreted into the bile and urine without conjugation. In addition, small amounts of products are from photo-oxidation. The wavelength, emission spectrum, and radiation delivered by the phototherapy device are among the controllable variables that can determine the effectiveness of phototherapy. In the new guideline for neonatal jaundice, an irradiance of at least 30 µW/cm^2/nm with a wavelength of 460 to 490 nm is considered safe to provide optimal therapeutic effect. Several studies have shown variability in spectral radiation among phototherapy devices, while irradiance footprint measurements are not performed in current clinical practice. As the photons of light are considered molecules of a drug, the pharmacological aspect of phototherapy has recently been proposed.

Methods: Here, we reviewed the studies on the effects of technical factors on the efficacy of phototherapy.

Results: There is a lack of studies about the suitability of irradiance in neonatal phototherapy devices. Limited studies in the Netherlands have investigated this issue. One study showed that the spectral irradiance of phototherapy devices is often lower than the manufacturer's specifications, and the high spectral irradiance footprints do not always cover the average body surface area required in a newborn. Another study measured irradiance levels of phototherapy devices used in 10 Dutch neonatal intensive care units. The mean irradiance level for phototherapy devices was 9.7 (4.3-32.6) µW/cm^2/nm. Approximately 50% of devices failed to meet the minimum recommended radiation level. Phototherapy devices in Dutch neonatal intensive care units showed considerable variability, with radiation levels often very low. A study in the United States showed improvement in the irradiance level with a standardized, multidisciplinary protocol specifying light arrangement and distance. On the other hand, a study in a neonatal intensive care unit in India showed that the relationship between the effectiveness

Key Words:
Phototherapy, Jaundice, Neonate

** Corresponding Author:*
Roya Farhadi, Associate Professor
Address: *Pediatric Infectious Diseases Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+98 (11) 33342334*
E-mail: *dr_royafarhadi@yahoo.com*

of phototherapy and the radiation level is likely non-linear. No studies have been conducted regarding the relationship of irradiance level with biochemical changes of bilirubin isomers, and there are only limited studies of the relationship of wavelength with photoisomerization. A study in Denmark showed that phototherapy with a wavelength of 497 nm vs 459 nm resulted in a different distribution of bilirubin isomers in neonates. In an in vitro study, the photodegradation of bilirubin and mainly the production of lumirubin was observed at a wavelength between 490 and 500 nm. Researchers in Japan succeeded in the standardization of phototherapy for neonatal hyperbilirubinemia using multi-wavelength radiation integration.

Conclusions: Irradiance level is an essential variable in the efficacy of phototherapy devices. Therefore, it is reasonable to measure and optimize an interdisciplinary team to improve the overall care of the neonate with hyperbilirubinemia. Further studies are needed to investigate the effect of multiple wavelengths and radiation levels on photochemical reactions of bilirubin.

Research Paper

Investigating Survival Rate in β-thalassemia Patients in Northern Iran During 25 Years: A Single-center Study

Hossein Karami[1*], Hadi Darvishi-Khezri[1], Aily Aliasgharian[1], Hanie Fallah[1], Maryam Hassanpour[1], Mobin Ghazaiean[1]

1. Thalassemia Research Center (TRC), Hemoglobinopathy Institute, Mazandaran University of Medical Sciences, Sari, Iran.

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ABSTRACT

Background: Thalassemia is one of the most common monogenic disorders of inherited hemoglobinopathies, requiring a multidisciplinary approach to medical management. This study investigates the role of factors affecting the survival rate of β-thalassemia patients.

Objectives: This study investigates the role of factors affecting the survival rate of β-thalassemia patients.

Methods: This retrospective study was carried out on 621 known β-thalassemia patients referred to the Thalassemia Research Center and Bouali Hospital for 25 years between 1991 and 2016. The demographic data, clinical findings, and laboratory tests alongside liver and cardiac T2*-weighted magnetic resonance imaging were measured.

Results: Of 621 patients, 315(50.7%) were female and 306(49.3%) were male. The median time of death for men was 21 years (n=27), while the age was 22 years for females (n=14; hazard ratio [HR]=1.15, 95% confidence interval = 0.6 to 2.23, PLog-rank test=0.65). Non-transfusion-dependent thalassemia (n=6) experienced a longer median time of death compared to transfusion-dependent thalassemia (n=35; 28 vs 21 years, HR=0.50, 95% confidence interval of 0.20 to 1.21, PLog-rank test=0.11). The splenectomized cases (n=35) demonstrated a greater median time to death than the non-splenectomized cases (n=6; 22 years vs 18 years, HR=1.46, confidence interval of 0.60 to 3.53, PLog-rank test=0.38). The mean time to death for hydroxyurea users (n= 9) was 28 years, whereas that was 21 years for the non-users (n=32; HR=0.64, 95% confidence interval of 0.30 to 1.35, PLog-rank test=0.23)

Conclusions: As per the estimated effect sizes, the role of gender in the mortality rate is negligible. Probably, non-transfusion-dependent thalassemia patients experience a longer life span compared to transfusion-dependent cases. Moreover, splenectomy is likely a risk factor for the rise in mortality rate, although the strength of the association is weak. Hydroxyurea was coupled with a plus point for the thalassemic users, bringing a lessened mortality rate to this population (nearly 46%). Notably, the study's results were not statistically significant and remained inconclusive as the sample size is exceedingly low, which calls for more robust studies

Key Words:

β-thalassemia, Survival rate, Splenectomy, Hydroxyurea

** Corresponding Author:*
Hossein Karami, MD.
Address: *Thalassemia Research Center (TRC), Hemoglobinopathy Institute, Mazandaran University of Medical Sciences, Sari, Iran.*
Tel: *+9`8 (11) 33347837*
E-mail: *karami_oncologist@yahoo.com*