Seyed Ali Malek Hosseini
Congress President

Dear All

I want to extend my most sincere and warm welcome to all distinguished guests and participants of "The 9th International Congress of Iranian Society of Organ Transplantation (IR-SOT)" in Shiraz, Iran.

Shiraz is renowned for its cultural heritage and historical importance. Near Shiraz are the spectacular remains of Persepolis, the capital of a vast empire built by Cyrus the Great, Darius, and Xerxes, whose names still echo through history. Other dazzling historic monuments can be visited in a short distance.

Following one year of hard work and constant efforts, the Organizing Committees are glad that it has fulfilled all the requirements for holding an excellent scientific meeting and abided by the suggestions and decisions made by the IRSOT Council.

We have tried to invite eminent scientific scholars and experts from around the world to attend this meeting in order to guarantee the high scientific richness of this gathering. IRSOT 2023 offers a unique opportunity to exchange new ideas in the field of transplantation medicine.

We have attempted to schedule the program such that the participants will have ample time to visit the exciting sightseeing spots of Shiraz and its vicinity, which are unique and unparalleled cultural and historic sites in our region. Also, during this congress, we will hold a "Great Ceremony of Life" in honor of family members of brain-dead patients.

We wholeheartedly wish participants a pleasant stay in this country and cherish the exemplary hospitality of the people of Shiraz while enjoying the rich cultural heritage of several millennia.

Seyed Ali Malek Hosseini

Congress President

Seyed Ali Malek Hosseini, Congress President

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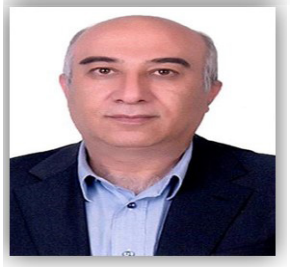

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RAPID Liver Transplant for Colorectal Metastasis

Mohsen Aliakbarian, MD

Transplant Research Center, Clinical Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran

ABSTRACT

Liver transplantation for colorectal cancer has once again piqued interest due to favorable overall survival outcomes in specific patient groups. However, the limited availability of donor organs poses a significant challenge to further exploring this area of transplant oncology. Utilizing small segmental auxiliary grafts from both deceased and living donors offers a potential solution to expand the donor pool without significantly affecting deceased donor transplant waiting lists or posing substantial risks to living donors.

This review offers insights into the physiological basis for this approach, outlines technical and surgical considerations, and summarizes the early experiences with this innovative concept. While international experience remains limited, initial short-term outcomes suggest the feasibility of this technique. However, there is insufficient long-term oncological data available.

The RAPID concept, involving resection and partial liver segment 2-3 transplantation with delayed total hepatectomy, remains an experimental surgical procedure. In this technique, first presented in 1990s, small segmental auxiliary grafts from living or deceased donors are used without negative impact for deceased donor pool and low risk for live donor. It should be reserved for prospective clinical trials. In this presentation, we discuss the key technical aspects of the RAPID procedure, both from deceased and living donors, and provide preliminary results from the first cases performed worldwide.

KEYWORDS: Liver transplantation; Colorectal metastasis; RAPID procedure

The Impact of Coronavirus Type 2 on Children with Liver Diseases

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ABSTRACT

The impact of comorbidities on the clinical presentation and outcome of SARS-CoV2 in children is poorly understood. This includes chronic liver disease, liver transplant recipients, and the use of immunosuppressive medication. Although children are not the main target of the virus, liver involvement has been observed in those infected with SARS-CoV2 and presenting with Multisystem Inflammatory Syndrome in Children (MIS-C). It is important to note that acute liver injury may occur in all children with SARS-CoV2 infection and those with chronic liver disease may experience hepatic decompensation. The diagnostic approach and general management strategies for children with SARS-CoV2 infection remain consistent regardless of CLD or previous liver transplantation (LT). Patients with and without pre-existing liver disease experience varying degrees of acute liver injury (ALI) due to potential mechanisms caused by SARS-CoV2 infection. Children with MIS-C may experience acute liver injury and elevated liver enzymes, which are typically self-limited. However, acute liver failure (ALF) has also been reported. Children who have end-stage liver disease may experience hepatic decompensation as a result of SARS-CoV2 infection.

Suspected or documented non-alcoholic fatty liver disease (NAFLD), including in obese children with CLD, may increase their risk for severe COVID-19. The role of SARS-CoV-2 infection in causing pediatric ALF leading to death or LT is uncertain and rare. Routine reduction or withdrawal of established immunosuppressive therapy is not recommended for children with autoimmune liver disease. However, reduction of immunosuppressive therapy can be considered based on general principles for managing infections in immunosuppressed patients. Following liver transplant in children, standard immunosuppression should not be reduced or withdrawn routinely even in mild or moderate SARS-CoV2 infection. Immunosuppression may not predict worse outcomes.

The decision to perform a liver transplant from a deceased donor who was infected with SARS-CoV2 into a child or to perform a liver transplant on a child who is infected with SARS-CoV2 should be made on a case-by-case basis. It is important to balance the risk associated with the underlying medical condition requiring the transplant against the risk of SARS-CoV2 infection.

There is currently not enough data to recommend the use of antivirals or immunomodulatory agents for treating COVID-19 in children with liver disease. It is highly recommended that children between the ages of 12 to 17 and suffering from chronic liver disease, including those with autoimmune liver disease and patients with cirrhosis, as well as transplant recipients, those on the waiting list for LT, and their caregivers, receive the SARS-CoV2 vaccination. The same recommendation applies to younger children, although safety is currently being evaluated.

KEYWORDS: COVID-19; Immunosuppression; Liver transplantation; Multisystem inflammatory syndrome in children; Chronic liver disease

Generation and Transplantation of Midbrain Dopaminergic Progenitors from Human Embryonic Stem Cells in Parkinson's Disease Models

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ABSTRACT

Parkinson's Disease (PD) is a common age-related neurodegenerative disorder with a rising prevalence. Human pluripotent stem cells have emerged as the most promising source of cells for midbrain dopaminergic (mDA) neuron replacement in PD. Here, we optimized and fine-tuned a differentiation protocol using a combination of small molecules and growth factors to induce mDA progenitors based on our clinical human embryonic stem cell (hESC) line to comply with good manufacturing practice (GMP) standards. The resulting mDA progenitors demonstrated robust differentiation and functional properties in vitro. Moreover, cryopreserved mDA progenitors were transplanted into 6-hydroxydopamine-lesioned rats, leading to functional recovery. Furthermore, scalability was demonstrated via transplantation in a parkinsonian monkey model. We therefore demonstrate that our optimized protocol using a clinical hESC line is suitable for generating clinical-grade mDA progenitors and provides the ground work for future translational applications.

KEYWORDS: Parkinson's disease; Pluripotent stem cells; Dopaminergic neuron

Management of Drug-Induced Hematological Complications after Solid Organ Transplantation

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ABSTRACT

Advances in the development of more effective immunosuppressive drugs have increased graft survival and drug induced adverse effects. Hematological complications, including neutropenia, thrombocytopenia, and anemia, occur frequently after solid organ transplantation (SOT), mostly within the first 100 days after transplantation surgery. The overall incidence of leukopenia/neutropenia has been reported to be 10-80%, which could increase the risk of opportunistic infections as well as graft rejection. Thrombocytopenia is another hematological side effect that has the greatest incidence in the first-year post SOT. The lowest platelet counts have mainly been reported within the first three months after SOT. Thrombocytopenia predisposes patients to mild to severe bleeding, bruising, malaise, and fatigue. Finally, the rate of anemia ranges from 20% to 51% during various time points after SOT, with the highest reported rate during the first-year following SOT. Anemia is an important predisposing factor for higher mortality rates, graft failure and cardiovascular complications such as left ventricular hypertrophy and congestive heart failure.

Drug-induced hematological complications need to be taken into account when all other probable causes have been excluded. Among the various medications, immunosuppressants remain the most probable cause, followed by antimicrobials. Most of these agents cause dose-related cytopenia, which resolves with dose reduction or drug withdrawal. However, any change in medications may result in negative consequences such as severe infections, bleeding, cardiovascular complications, acute allograft rejection, and graft or patient loss.

Due to the lack of high quality randomized controlled trials, cautious evaluation of the patient's condition, transplant risk factors and pharmacological properties of the medications is required for the identification and management of drug-induced hematological complications after SOT.

KEYWORDS: Immunosuppressive drug; Hematological complications; Solid organ transplantation

COVID-19 Vaccines in Solid Organ Transplant: What Have We Learned?

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ABSTRACT

None of the recently rolled out COVID-19 vaccines has been rigorously tested in solid-organ transplant recipients (SOTR). The original vaccines trials were not designed to assess viral transmission, disease severity or death as primary outcomes, and many high-risk subgroups such as SOTR were excluded. Vaccine-induced neutralizing antibodies levels in immunocompetent individuals decline shortly after vaccination and are partially protective against new variants in spite of boosting. SOTR have considerably lower seroconversion rates and antibody titers after full vaccination. Various SOTR seroconvert after SARS-CoV-2 infection and their T cell responses are similar to those in healthy individuals. Risk factors for poor vaccine immunogenicity include old age, comorbidities, shorter time from transplantation, use of mycophenolate, Belatacept and worse allograft function. Correlate of immunity against the SARS-CoV2 remains unidentified. Interestingly, spike-specific T cell responses are detected in a sizable proportion of seronegative individuals. Clinical markers and immune cutoffs for protection from severe COVID-19 are currently unknown regardless of immune status. In the absence of any well-defined correlate of immunity, assessment of COVID-19 vaccines immunogenicity remains an important challenge in SOT. Consequently, short and long-term clinical efficacy, immunogenicity, time span of immune protection and safety data on COVID-19 vaccines are currently lacking. Early cardiovascular, autoimmune and neurological adverse events and even augmented risk of early death following vaccination are increasingly acknowledged. Most of the current recommendations in SOTR are based on expert opinion from limited single center observational data, retrospective analysis or extrapolation from studies in the healthy population. The experimental nature of the vaccines, their recently confirmed serious adverse events and inability to stop viral transmission, should have made the informed consent mandatory rather than the scientifically and legally unfounded sanitary pass. This appraisal stresses the need for future well-designed trials to characterize COVID-19 vaccine immunogenicity, efficacy and safety in this patients' population.

KEYWORDS: COVID-19; Vaccination; Solid organ transplantation

Critical Management of Antibody-Mediated Rejection among Liver Transplant Recipients

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ABSTRACT

Liver is considered immune-privileged due to a high capacity of immune tolerance; however, antibody-mediated rejection (AMR) has gained clinical alertness recently as a potential cause of chronic liver allograft injury, fibrosis and failure. The incidence of biopsy proven AMR is 0.3-2% in ABO-compatible liver transplant (LT) patients. It is more common in pediatrics, sensitized, and ABO incompatible LT. Among 1503 adult and 113 pediatric LT recipients at IKHC center, Tehran, Iran, AMR was reported in 7 adult (0.47%) and 5 pediatric LT patients (4.42%). In addition to augmentation of maintenance immunosuppression and increasing patient's adherence to drug therapy, the main treatment of AMR is based on two complementary approaches: 1) removal of harmful antibodies from the blood through plasmapheresis or immunoadsorption and 2) modulation of various components of specific and/or innate immunity using IVIG, anti-CD20 mono clonal antibodies (mAb), rabbit anti-thymocyte globulin, proteasome inhibitors, anti-C5 antibodies and other new mABs. IVIG multimodal function includes interference with B- and T-cell activation, antibody formation and recycling, as well as complement activation. CD20 mAbs (rituximab and obinutuzumab) are B-cell depleting and promote cell lysis by triggering the complement dependent and antibody-dependent cytotoxicity. Obinutuzumab has more profound B-cell depletion than rituximab. Proteasome inhibitors (bortezomib and carfilzomib) induce apoptosis of bone-marrow-derived plasma cells and lead to the reduction in alloantibodies production. One issue with bortezomib (and possibly carfilzomib) was the rebound injury reported in AMR of KT recipients. There are reports of using bortezomib in LT patients with AMR. Carfilzomib is a second generation, irreversible proteasome inhibitor. Experience with carfilzomib for treatment of AMR is in lung transplantation and cases in pediatric kidney transplant patients. Although anti-C5 mAb (Eculizumab) has been effective for liver transplant AMR in animal models, clinical case report showed no effect. IL-6 inhibitors (e.g., clazakizumab) and IL-6R inhibitors (e.g., tocilizumb) block the action of IL-6 either directly or at the receptor level, respectively. Blockage of IL-6 leads to inhibition of the maturation of naïve CD4+ T-Cells into CD4+ Tfh and TH17, which inhibits autoimmunity and decreases antibodies production, and upregulates differentiation into CD4+ Tregs, which suppresses inflammatory response. The blockage of IL-6 also inhibits the differentiation of naïve B-Cells to plasma cells and memory B-Cells producing donor specific antibodies (DSAs). These drugs have been used for AMR treatment in heart and kidney transplant patients. Up to now, there is no clinical experience with them for AMR treatment in LT patients. CD38 mAb (daratumumab) and anti-B lymphocyte stimulator monoclonal antibody (belimumab) are other mAbs that are studying in AMR treatment in organs other than the liver.

KEYWORDS: Antibody-mediated rejection; Liver transplantation; Allograft injury

Immune Tolerance in Pediatric Liver Transplantation

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ABSTRACT

The optimal level of immunosuppression in solid organ transplantation is a delicate balance between the benefit of preventing rejection and the adverse side effects of immunosuppression.

Liver transplant does not require HLA matching between donor and recipient and also simultaneous transplant of liver with another solid organ decreases the incidence of rejection episodes for the second organ. Liver Transplant recipients are maintained on lower levels of immunosuppression than other solid organs.

Usually, a calcineurin inhibitors, alone or with an anti-proliferative agent mycophenolic acid or azathioprine is started early post transplantation in combination with a corticosteroid to help maintain immunosuppression. Tacrolimus based regimen is superior to cyclosporine based with significant improvement in patient and graft survival, less rejections, less hypertension and decreased dose of required corticosteroids.

Other immunosuppressant agents as MMF or mTORIs may be used in pediatric liver transplant for specific indications. T-cell depleting antibodies such as ATG and IL-2Ra are increasingly used in children by some liver transplant centers for indications similar to adults.

The unique immune tolerant character of the liver (Liver Tolerance) makes total withdrawal of immunosuppression potentially possible in these cases.

The aims of withdrawal of immunosuppression are to minimizing the adverse side effects and improving the quality of life.

Weaning of immunosuppression may be possible in up to 40% of liver recipients. The success rate of weaning may be even higher in pediatric patients receiving parental organs.

The most important factor affecting the success rate of immunosuppression withdrawal in liver transplant recipients is the time from transplantation. Other implicated factors include the male gender, older age at the time of transplantation, and indexes of lymphocytes stimulation.

It should be considered that candidates for immunosuppression weaning have been carefully selected in most studies among patients with non-immune causes of liver disease, stable post transplantation liver function, and less rejection episodes.

KEYWORDS: Immune tolerance; Pediatrics; Liver transplantation

Novel Immunosuppressive Agents in Solid Organ Transplantation

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ABSTRACT

Immunosuppressive drugs used in the transplantation period are generally defined as induction and maintenance therapy. The use of immunosuppressants, which are particularly useful and have fewer side effects, decreased both mortality and morbidity. Many drugs such as steroids, calcineurin inhibitors, antimetabolites, and mTOR inhibitors are used as immunosuppressive agents. Although immunosuppressant drugs cause many side effects such as hypertension, infection, and hyperlipidemia, they are the agents that should be used to prevent organ rejection. This shows the importance of individualized drug therapy. The optimal post-transplant immunosuppressive therapy is not established. Therefore, discovering less toxic but more potent new agents is of great importance, and new experimental and clinical studies are needed in this regard. Imlifidase, the IgG-degrading enzyme derived from Streptococcus pyogenes, is a recombinant cysteine protease that cleaves all four subclasses of human IgG into F(ab')2 and Fc fragments, inhibiting complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity. Imlifidase has received conditional approval by the European Medicines Agency for desensitization in kidney transplantation. Imlifidase is not yet US Food and Drug Administration approved for use in the United States. Clazakizumab, a humanized anti-IL-6 monoclonal antibody, was initially being developed as a treatment for rheumatoid arthritis but is presently being investigated as a treatment for chronic active ABMR in kidney transplantation. Obinutuzumab is a third-generation anti-CD20 monoclonal antibody. In contrast to rituximab, B cell death with obinutuzumab is less reliant on CDC and is mediated primarily through antibody-dependent cellular cytotoxicity. Both rituximab and obinutuzumab effectively deplete B cells in the peripheral blood; however, obinutuzumab more effectively depletes B cells in the secondary lymphoid organs and may have more lasting effects on memory B cells and plasma cells due to its mechanism of action. Belimumab, a human monoclonal antibody that inhibits the soluble form of B lymphocyte stimulator (BlyS), has been proposed for prevention of antibody-mediated rejection (ABMR). High serum concentrations of BLyS in kidney transplant recipients have been associated with the development of de novo donor-specific anti-human leukocyte antigen (HLA) antibodies (DSA), high concentrations of HLA antibodies, and an increased frequency of ABMR. CFZ533, fully human glycosylated immunoglobulin G1, inexhaustible anti-CD40 antibody blocks CD154 binding to CD40 and downstream pathway activation. It prolongs renal allograft survival and function when administered as monotherapy in the primate's model. It may be used an alternative to calcineurin inhibitor treatment regimens in clinical transplantation. Voclosporin, a novel oral semisynthetic analog of cyclosporine that inhibits calcineurin, is as potent as tacrolimus and similar in renal allograft function preservation and is also thought to be associated with a reduced incidence of new-onset diabetes. Efalizumab is a humanized anti-CD11a monoclonal antibody directed against lymphocyte function associated antigen 1 (LFA1). The binding of efalizumab to LFA1 inhibits the adhesion and trafficking of leukocytes without lymphocyte depletion. It has been promising option for organ rejection prevention. Sutimlimab selectively blocks the classical pathway of complement-specific serine protease C1s to prevent the formation of the classic C3 convertase pathway. A single-arm pilot trial showed that it is effectively blocks the alloantibody-triggered classical pathway activation in kidney transplant recipients.

KEYWORDS: Novel immunosuppressive agents; Solid organ transplantation; Maintenance therapy

Immersive Experience: Family Approach for Organ Donation

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ABSTRACT

As we know brain dead family's refusal for organ donation is one of the biggest obstacles in the organ donation process.

There are about 20 reasons for family refusal for organ donation in the world, the order of which varies depending on that country's society culture, the laws, the economic situation, etc., and these twenty reasons can be divided into two main categories. Which include:

- Not accepting brain death as death

- Reluctance to donate an organ

Based on researches conducted in the world, it can be said conclusively that the most important causes in the world are related to the first category or the disbelief that brain death is irreversible.

There are two solutions to this problem:

1- Continuous cultural activities to change the beliefs of that society; which is a long-term process and may take several decades and requires the interaction of the health system, people in the community, celebrities, and cultural organizations and institutions.

2- Training professional coordinators with the necessary information to deal with the affected families of brain dead people who are in the most bitter and critical moments of their lives to break the bad news and request organ donation, and not let them suffer additional psychological damages.

Naturally, the second solution, until society reaches its most ideal point, which is the acceptance of brain death as death and the desire to donate organs, is the best and fastest way to increase organ donation consent rate and provide more transplant organs to the community.

We should keep in our mind that nowadays family approach is a science with many specific technics should be learned; combination of psychology, sociology and public relation; not just an intuition.

So, it is our main motto that: not approaching to the family is better than approaching by an untrained person.

Because incorrect approach not only can makes a chronic grief for the family but also can put the needy patient's lives in danger.

KEYWORDS: Family's refusal; Organ donation; Brain death

Results of Pediatric Kidney Transplants in an 8-Year Period: A Retrospective Study

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ABSTRACT

Background: Patient survival and quality of life is better after a kidney transplant compared with dialysis. In this retrospective study, we analyzed the results of pediatric kidney transplants in an 8-year period in our center.

Methods: We reviewed the files of 166 children and adolescents who had undergone kidney transplants between 2008 and 2015 in our center. All the patients were younger than 18 years old and had been followed up for at least 2 years.

Results: The transplanted kidneys were taken from live donors in 146 (88%) of the cases and from cadavers in 20 (12%) of the cases. They were procured from unrelated and related donors in 129 (90%) and 17 (10%) of the cases, respectively. Laparoscopic nephrectomy was done on 141 donors. The kidney vessels were anastomosed to the aorta, the common iliac, and the internal iliac in 3.6%, 56%, and 40.4% of cases, respectively. Preemptive kidney transplants were performed on 62 patients. The mean of patient survival was 124±1.37 months. One- and five-year patient survival rates were 99% and 97%, respectively. The mean of graft survival was 118.29±2.47 months. One- and five-year graft survival rates were 94% and 93%, respectively. Preemptive kidney transplants had a higher graft survival rate ($P<0.02$).

Conclusion: Kidney transplant is a safe and feasible procedure in children and adolescents based on patient and graft survival outcomes. In our center, surgery complications led to kidney loss in very few cases.

KEYWORDS: Pediatrics; Kidney transplantation; Survival rate; Quality of life

Development of Organ Transplantation in Turkey: From Past to the Future

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ABSTRACT

The cornerstone events of organ transplantation history in Turkey are summarized herein. Solid-organ transplantation in Turkey began with two heart transplants in 1968. By the early 1970s, experimental studies on liver transplantation had been initiated by our team when I was a third year surgical resident.

Following these attempts, **the first living related kidney transplant in Turkey was conducted on November 3, 1975 for a 12-year-old male patient from his mother by our team.** At that time, there were no legislation governing transplant activities in Turkey. In an attempt to start a deceased-donor donation program in Turkey, I worked in cooperation with international networks, including Eurotransplant Foundation and South Eastern Organ Procurement Foundation. Thus, **we performed the first deceased-donor kidney transplantation on October 10, 1978, using an organ supplied by the Eurotransplant Foundation. These kidneys were used with a high success rate** and I proved that **deceased kidneys with more than 100 hours cold ischemia time could be successfully transplanted.**

As a result of our efforts, the law on harvesting, storage, grafting, and transplantation of organs and tissues was enacted on June 3, 1979. **This law has been a milestone in the development of organ donation and transplantation in Turkey.** Once the **Law No. 2238** was passed, we performed **the first local deceased donor kidney transplantation on July 27, 1979.**

I founded The Turkish Organ Transplantation and Burn Treatment Foundation in 1980 to promote organ donation. On January 21, 1982 some new articles were added to Law 2238, with the enactment of Law 2594, which allowed for deceased donation without consent from next-of-kin.

This was followed by a period of many groundbreaking events. **The first successful deceaseddonor liver transplantation was performed in Turkey, in the Middle East and in Northern Africa on December 8, 1988 again by our team. This was followed on March 15, 1990 with the first pediatric segmental living-related liver transplant in Turkey, the region, and in Europe and succeeded by the first adult segmental living-related liver transplant (left lobe) in the world on April 24, 1990. On May 16, 1992, we performed combined liver-kidney transplant from a living-related donor, which was the first operation of its kind in the world.**

In addition, we conducted heterotopic liver transplantations. **In 1998, we performed heterotopic deceased-donor partial liver transplantation to a 17-year-old girl, heterotopic living-related transplantation to a 16-year-old boy and heterotopic living-related liver transplantation to a 17-year-old boy from his mother in 1999.**

According to our donor selection criteria, all candidates should be relatives (up to the fourth degree) or the spouse of the recipient and ≥ 18 years old. Between November 1975 and September 2023, 3490 kidney transplants (407 pediatric, 3083 adult) from living = 2754 and deceased = 736 donors were performed and 745 liver transplants (366 pediatric, 379 adult) from living = 528 and deceased = 217 donors were performed.

In 2001, the Ministry of Health established the National Coordination Center to promote transplantation activities, especially for deceased donor organ procurement. Today, deceased donors are still far below the desired rates. Efforts to increase awareness continue through media, schools, and many public and private institutions.

The main goal should be to promote organ donation from deceased donors and to fight against living unrelated transplantation. This is the most efficient way to eliminate commercial transplantation and transplant tourism.

KEYWORDS: Solid organ transplantation; Turkey; Law No. 2238; deceased donors

Gastrointestinal (GI) Post-transplant Lymphoproliferative Disease (PTLD) in Patients underwent Liver Transplant

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ABSTRACT

Post-transplant lymphoproliferative disorder (PTLD) is a serious complication that can occur after solid organ transplantation and hematopoietic stem cell transplantation. Gastrointestinal (GI) PTLD is a subtype of PTLD that affects the GI tract. It is characterized by the uncontrolled proliferation of lymphoid cells in the GI mucosa and submucosa. GI PTLD can present with a variety of symptoms, including abdominal pain, nausea, vomiting, diarrhea, and gastrointestinal bleeding. It can be caused by uncontrolled proliferation of Epstein–Barr virus-positive B-cells in the setting of chronic immunosuppression. As one of the biggest transplant centers worldwide, we observed a potential increase in the number of patients with posttransplant lymphoproliferative disorder presenting with gastrointestinal symptoms recently. There is limited information about dysregulation of the immune system following coronavirus disease 2019 infection, which may lead to Epstein–Barr virus reactivation in Epstein–Barr virus-positive B-cells and development of posttransplant lymphoproliferative disorder. Furthermore, there is no consensus in literature on a modality that can help in early diagnosis of posttransplant lymphoproliferative disorder with nonspecific gastrointestinal presentations before late and fatal complications occur. The diagnosis of GI PTLD is challenging and requires a combination of clinical, radiological, endoscopic, and histological findings. Treatment options for GI PTLD include reduction of immunosuppression, chemotherapy, radiation therapy, and surgery. The prognosis of GI PTLD depends on various factors, including the type and extent of the disease, the patient's age and overall health status, and the response to treatment. Early detection and prompt management of GI PTLD are crucial for improving patient outcomes.

KEYWORDS: Post-transplant lymphoproliferative disorder; Epstein–Barr virus; Gastrointestinal tract; Liver transplantation

Pre-transplant Nutritional Assessment in Pediatric Patients with End-stage Liver Diseases.

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ABSTRACT

Malnutrition is a common complication of chronic liver diseases at all ages, particularly in pediatric patients. It depends on several cooperating factors such as poor nutrient intake, malabsorption and/or maldigestion, increased energy needs and endocrine dysfunction.as malnutrition is suggested to increases the mortality and morbidity and significantly influences the outcomes of liver transplantation, all children with liver disease should have a clinical nutritional evaluation with an intervention and follow-up plan appropriate for the patient's status. The evaluation of the nutritional status of these patients is based on anthropometric, biochemical, and instrumental indicators. Among anthropometry measurements, stunting which is determined by serial measurements of the height–age index (height-for-age ≤ −2 SD of the WHO child growth standards median) may be a good indicator of chronic malnutrition, while short-term changes in nutritional status need to be tracked using other parameters such as the mid upper arm circumference (MUAC) and triceps skin fold (TSF). Serum protein levels (albumin, prealbumin, transferrin, and retinol-binding protein) alone cannot be used as an indicator of malnutrition, as their production is influenced by hepatic disease, sepsis, inflammation, and hydration status. Prealbumin is a more sensitive marker for the severity of malnutrition and/or adequacy of nutritional support; it has a half-life of 2 days, low body reserves, responds quickly to nutritional status, and its production in the liver is maintained until late in liver disease. The evaluation of nutritional status in children also includes instrumental investigations that assess body composition: dual-energy X-ray absorptiometry (DXA), bioelectrical impedance (BIA), and indirect calorimetry. Nutritional needs of children with chronic liver diseases are suggested as follow in recent guidelines: for macronutrients, Energy intake of about 130–150% estimated average requirement (EAR), Protein intake of 9% of total energy equal to about 3–4 g/kg/day, Fats intake of 40% of total energy, 10% of which as long chain PUFA to cover essential fatty acids, with 30–50% as MCTs, Sodium intake is 1 mmol/kg/day and potassium about 2 mmol/kg/day. To cover micronutrients needs due to malabsorption, fat soluble vitamins supplementation such as Vit A (3000–10,000 IU/day), Vit D3 (Cholecalciferol: 800–5000 IU/day), Vit E (Alpha-tocopherol acetate: 25–200 UI/kg/day, And Vit K, 2.5–5.0 mg/day from twice a week to every day.

The complex dietary management for this type of malnourished patient requires the aid of a specialist dietitian, educational training regarding nutritional guidelines for stakeholders, and improving family nutritional health literacy, besides improvement in nutritionally complete formulas.

KEYWORDS: Pediatrics; Nutritional assessment; Nutritional need; Liver diseases

BK Virus in Kidney Transplantation

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ABSTRACT

BK Polyomavirus (BKPyV) is a non-enveloped double- stranded DNA virus that is a member of polyoma subgroup of papova viruses, which includes JC virus and SV40. Infection with BK virus is common in the general population, with an estimate of seropositivity in adults by 80%- 90%. After resolution of primary infection, BK virus remains latent in several locations throughout the body, most notably within the genitourinary system.

During immunosuppression, the virus may become reactivated and begin to replicate. After the introduction of potent immunosuppressive medications in the late 1990s, BK virus viruria was reported in up to half of renal allograft recipients in the first few months, but only 10%-15% of patients developed viremia. Progression of viremia is thought to be a prerequisite for the development of BK virus nephropathy (interstitial nephritis and ureteral stenosis after kidney transplantation)(BKVN); about 3%-5% of allografts were being lost due to BKVN. Transplant kidney biopsy remains the gold standard for diagnosing BKVN. There is no definite treatment for BK virus (BKV) infection including: BKV nephropathy. Studies that look for risk factors responsible for BKVN have shown inconclusive results.

The human BK polyomavirus is associated with two significant complications in transplant recipients: polyoma virus associated nephropathy (PyVAN) in 1-10% of kidney transplant recipients and polyomavirus-associated hemorrhagic cystitis (PyVHC) in 5-15% of hematopoietic stem cell transplant (HSCT) patients.

Although JC virus (JCV) inhabits in the uroepithelium and during the periods of immunosuppression may be reactivated, It rarely causes nephropathy but could lead to progressive multifocal leukoencephalopathy (PML). After kidney transplantation, under the state of immunosuppression BKV replication starts and progresses through detectable stages: Viruria, viremia and then nephropathy.

In reviewing the articles for screening BKV infection after kidney transplantation, different methods for finding BKV are provided by articles, the choice of which depends on the policy of the kidney transplant department and economic issues.

These tests vary from finding decoy cells (Fig. 1), in the urine (sensitivity 100%- specificity 45%), to measure the BK viral load in the urine and blood. However, measuring BK viral load has a higher value (sensitivity 100%- specificity 66-90%) depending on viral load more than 10,000 copies/ml in blood (Fig. 2).

Polyomavirus infection is a serious threat for the life of transplanted kidney. It could occur at any time post transplantation and cause an increase in plasma creatinine level silently. Also, it may lead to irreversible tubulointerstitial changes in transplanted kidney and then loss of the graft. Table 1 shows risk factors for BK virus reactivation and BK virus-associated nephropathy.

BK polyomavirus replication in renal tubular epithelial cells is inhibited by Sirolimus, but activated by Tacrolimus through a pathway involving FKBP-12.

KEYWORDS: BK virus; Kidney transplantation; Nephropathy

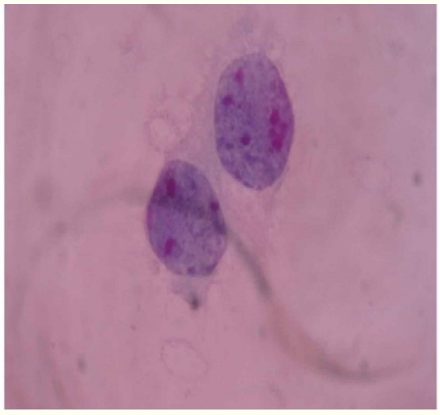
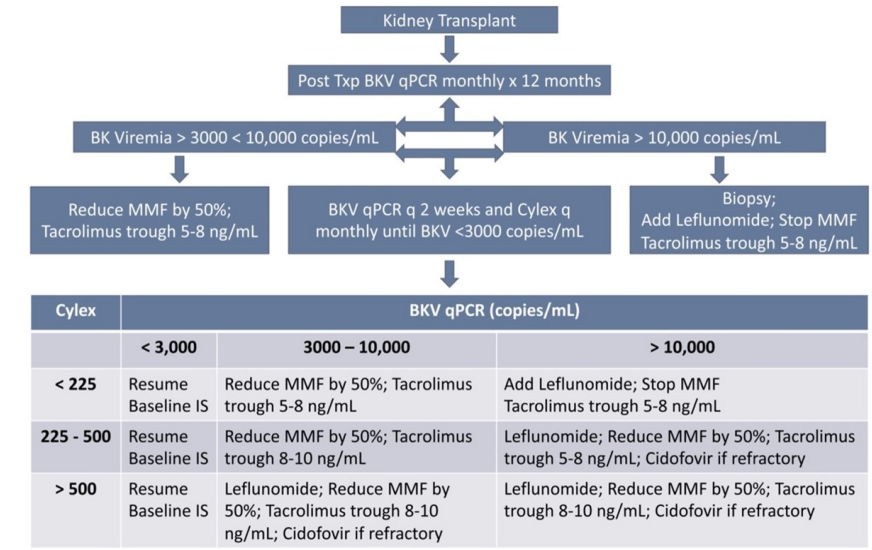


Figure 1: Decoy cells in urine.



Cylex	BKV qPCR (copies/mL)		
	< 3,000	3000 – 10,000	> 10,000
< 225	Resume Baseline IS	Reduce MMF by 50%; Tacrolimus trough 5-8 ng/mL	Add Leflunomide; Stop MMF Tacrolimus trough 5-8 ng/mL
225 - 500	Resume Baseline IS	Reduce MMF by 50%; Tacrolimus trough 8-10 ng/mL	Leflunomide; Reduce MMF by 50%; Tacrolimus trough 5-8 ng/mL; Cidofovir if refractory
> 500	Resume Baseline IS	Leflunomide; Reduce MMF by 50%; Tacrolimus trough 8-10 ng/mL; Cidofovir if refractory	Leflunomide; Reduce MMF by 50%; Tacrolimus trough 8-10 ng/mL; Cidofovir if refractory

Figure 2: Monitoring and treatment protocol for BK virema.

Table 1
Risk factors of BK virus reactivation and BK virus–associated nephropathy

Risk Factors of BKV Reactivation After Transplantation		
Recipient-Related	**Donor-Related**	**Transplant-Related**
• Older age	• Female gender	• High immunosuppression drug levels
• Male gender	• African American	• Use of tacrolimus
• Steroid exposure	• Deceased donors	• Thymoglobulin induction
• Antirejection treatment	• BKV seropositive status	• Ureteral stents
• Diabetes mellitus		• HLA mismatch
• Negative BKV serostatus		• A,B, OR O blood groups incompatibility
		• Ischemia or reperfusion injury
		• Long ischemia time

Figure 3: Management of BKPolyomavirus Infection in Kidney and Kidney-Pancreas Transplant Recipients.

Liver Transplantation for Secondary Liver Tumours: Is It Worth Doing?

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ABSTRACT

The standard treatment of liver secondaries consists of the combination of chemotherapy and liver resection. There has been a renewed interest in considering liver transplantation (LT) as a therapeutic option in the treatment of well selected, neuro-endocrime (NET-LM) and colorectal (CR-LM) liver metastases.

NET are often diagnosed at an advanced stage. Fortunately the metastatic disease often remains confined to the liver for a long period, so R0 primary tumour resection followed by liver resection may represent a curative option. The ELTR and the INT in Milan experiences revealed that total hepatectomy (read LT) may be of value in the treatment of non-resectable NET-LM when following selection criteria are respected : R0 resection of the primary tumour, presence of a well differentiated, low-grade tumour[Ki-67 < 5 –10 %]; primary tumour localization within the portal venous drainage area; tumour burden < 50 % of liver volume; age < 55 years; response to somatostatin analogues and m-Tor inhibitors; stable or controlled disease for ≥ 6 months and avoidance of multivisceral transplantation. Excellent 5-years overall (OS) as well as disease free survival (DFS) rates (ranging from 92 to 79 % and 75 to 57 %) can then be obtained.

More recently the Oslo SECA 1 and 2 studies triggered the interest for the role of LT in the treatment of non-resectable CR-LM. CEA <80 µg/L, delay between primary tumour and occurrence of metastases over 2 years, largest tumour diameter <5.5 cm, and stable disease under chemotherapy have been identified as favourable factors in relation to outcome. In the SECA-1 trial , one-year DFS reached 35%: adjuvant surgery raised the 5-yeas DFS to 60%. In the SECA-2 study, PET-CT imaging was added as a selection criterium. One- and 5-years OS and DFS reached 100% and 83% and 53% and 35%,. These encouraging results resulted in several trials in France, Italy and Canada. It is also interesting to note that immunosuppression did not have a negative impact on the growth of recurrences and that immunosuppression and chemotherapy can be combined safely. Living donor LT (LDLT) undoubtedly will play a role in the development of this field because not interfering with the scarce allograft resource and allowing adequate timing of LT within the oncologic treatment. Our initial experience with 24 LM-recipients showed that LDLT favourably compares to deceased donor LT and that the absence of portal hypertension makes both donor and recipient surgeries safe because allowing to combine the small left-liver and graft inflow modulation. Time has come to fully integrate LT into the therapeutic algorithm of non-resectable secondary liver tumours.

KEYWORDS: Liver transplantation; Secondary liver tumours; Therapeutic algorithm

Liver Transplantation and Hepatocellular Cancer: How Far Can (Should) We Go?

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ABSTRACT

Although based on morphologic criteria only (number and diameter) , the Milan and University of California San Francisco (UCSF) still remain the international gold standard to select hepatocellular cancer (HCC) patients for liver transplantation (LT) although introduced in clinical practice in 1996 and 2001 respectively.

After some years of stabilized practice, it became clear that these criteria were much too strict, denying access for many patients to a potentially curative therapy. Many Western teams worked at a cautious extension of the inclusion criteria, conversely, many Eastern centres adopted a much more aggressive attitude fostered by the explosive development of living donor liver transplantation (LDLT). Indeed LDLT was and is thé fertile soil to explore the widening of transplant indications in HCC patients not only because of allowing a better planning of the surgical procedure but even more because avoiding to interfere with the scarce deceased donor pool.

In 2007, the Kyoto group demonstrated for the first time that the morphology-alone selection approach was overruled by two fundamental principles of modern oncology, namely the necessity to combine tumour morphology and biology and to evaluate the response to neo-adjuvant locoregional therapies (LRT) allowing to address tumour aggressivity and behaviour. Both arguments are very powerful predictors of the oncologic outcome of HCC liver recipients.

A systematic review of the literature, covering the period 1993 (date of the first reported HCC-LT score) -2022, identified not less than 56 (!) different inclusion criteria/ scores of HCC for LT. This high number of scores very well reflects the dissatisfaction of the transplant community with the merely, restrictive allograft allocation rules.

This lecture will focus on the justified extension of inclusion criteria based on the combination of, both morphologic and biologic, dynamic tumor characteristics, highlighting thereby the role of tumor markers (AFP, DCP or PIVKA II), inflammatory markers (neutrophil- (NLR) and platelet-to-lymphocyte (PLR) ratios), tracer-uptake at PET-CT scanning and radiological response to neo-adjuvant LRT in the selection process for LT.

The development of a widely accepted “comprehensive” HCC-LT score becomes a necessity together with wider implementation of LDLT in order to offer the best possible treatment to the highest possible number of HCC patients.

KEYWORDS: Liver transplantation; Hepatocellular cancer; Neo-adjuvant locoregional therapies

How DCD Can Improve Deceased Donation and Transplantation Programs

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ABSTRACT

Today is already demonstrated that donation after circulatory death is a complementary source of donors in many countries worldwide. 23 countries have been implementing this technique in the last 10 years and that fact represents that from total deceased worldwide, 22.2% are DCD.

The most common way we call it "controlled" DCD -. That means death after withdraw the treatment of patients in the critical care situation, however, for the future , we suggest that the main source of donors will come from the uncontrolled DCD because the first etiology of death worldwide is ischemic cardiopathy that happens outside of the hospital and with rescue systems and plus mobile teams and plus all the technologies, some of these organs can be utilized for transplantation.

At the beginning of these programs it was too hard to evaluate the viability of these organs but today is quite mandatory to implement the technique of normothermic regional perfusion (NRP), as we published in the year 2000, and today amplificated with touraco abdominal heart and lung retrieval. That means to change the metabolism to anaerobic after ischemia damage for cardiocirculatory death to aerobic conditions so we can evaluate the organ function before doing the retrieval and to assess the viability.

Nevertheless also in the last years we have seen many devices to check the organ viability, to try to recuperate the function, to implement the logistics for transplantation and to other treatments that we will have in the future and that is the ex situ perfusion machine for all the organs that is today in clinical trials and research phase.

The utilization of the organs from DCD donors today is implemented for all organs, for kidney mainly, as well for liver, lung for heart for pancreas with excellent results compared from organs provided from DBD . The importance in our area of these source of donation means that Spain with 45 donation pmp , 27 pmp had been form DBD and 19.2 pmp from DCD , and if we look at my region Catalonia then the 54% of the total donation comes from DCD, and the rest from DBD. So today the main source of donors in Barcelona region is Donation after circulatory death. Thanks to that we can maintain the access to transplantation to all patients in our waiting list.

KEYWORDS: Organ donation after cardiac death; Deceased donation; Transplantation programs

How to Develop Deceased Donation Worldwide

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ABSTRACT

We are aware that worldwide there is lack of organs and today we can only achieve the 10% of the global needs in transplantation, even using living donation from liver and kidney because we have only 38.000 donors worldwide per year.

What are the solutions? Our proposal is that nations should support by regulating, laws and legislation and the regions must implement the health systems including developing of deceased donation and basically, as shown in other countries like Spain, Iran, Portugal, Italy, France, etc, to have an hospital structure with organ procurement units, is the main factor to develop Deceased Donation. And that is the TOP 5 models in the world, including USA with a different model which is a OPO system.

TPM is a medical specialist in ICU supported by nurses , dedicated 24h/7days to organ donation, could be a single person or a professional team and the main issue is that depends from the hospital medical direction , it is a social responsibility for any hospital to perform that, and those professionals do the clinical activity, they do the research, they do the quality , they do the management to analyze the cost, as well as training or education.

From our point of view there is no single demonstration that by only changing legislation, awareness campaigns, donor registries, driving license or other way of promotion, donation has increased.

We believe that one professional trained by the health system is the same of 2000 citizens aware of organ donation. Thus, the development of programs to professionalized people has shown in many areas in Europe, in Iran, in China in Emirates and worldwide good results: as many professionals trained, more the donation rates increase.

Finally, during more than 25 years, we have been implementing this in Spain and we have achieved the point of self-sufficiency, that means that our waiting list at the end of the year remains stable of the previous years. So, all the patients in the waiting list have the great opportunity to get transplanted.

In addition, for example in Catalonia (region) , the 54% of the patients with chronical kidney disease are transplanted and the other in dialysis, and even the 7% of these patients are preventive transplanted before dialysis.

In conclusion the implementation of the TPM professionals inside the hospitals is the key solution to develop deceased donation Worldwide.

KEYWORDS: Deceased donation; TPM professionals; Health system

Mycobacterial Infections and Kidney Transplantation

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ABSTRACT

Mycobacterium tuberculosis (MTB) infection is a major public health problem worldwide, and renal transplant recipients are at an increased risk of developing active tuberculosis (TB) disease. The prevalence of latent tuberculosis infection (LTBI) in renal transplant recipients is estimated to be 10-20%, which is significantly higher than the general population. The risk of developing active TB disease is highest in the first year after transplantation and declines over time. However, the risk remains elevated throughout the lifetime of the transplant recipient.

Several factors contribute to the increased risk of TB in renal transplant recipients, including:

- Immunosuppressive therapy: Immunosuppressive medications used to prevent transplant rejection suppress the immune system, making it more difficult for the body to fight off TB infection.
- Underlying kidney disease: Chronic kidney disease (CKD) is a risk factor for TB infection, even without transplantation.
- Comorbidities: Other comorbidities such as diabetes, malnutrition, and HIV infection also increase the risk of TB in renal transplant recipients.

The clinical manifestations of TB in renal transplant recipients can be non-specific and difficult to distinguish from other infections. However, some common symptoms include fever, night sweats, weight loss, cough, shortness of breath, hemoptysis, flank pain, dysuria, frequency, urgency, and nocturia.

The diagnosis of TB in renal transplant recipients can be challenging due to the non-specific nature of the clinical presentation and the potential for false-negative results on diagnostic tests. The diagnosis is typically based on a combination of clinical findings, laboratory testing, and imaging studies.

Once the diagnosis of TB is confirmed, the patient should be started on appropriate anti-tuberculous therapy. TB treatment in renal transplant recipients can be complex, and it is important to balance the risks and benefits of different treatment regimens carefully.

KEYWORDS: Mycobacterium tuberculosis; Chronic kidney disease; Immunosuppressive therapy

mTOR Inhibitors in Pediatric Liver Transplantation

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ABSTRACT

Pediatric liver transplantation is a critical procedure that saves the lives of children with end-stage liver disease. The most frequently used immunosuppressive regimens following pediatric liver transplantation are centered around calcineurin inhibitors (CNIs), with tacrolimus being the preferred choice. While CNIs have greatly improved patient outcomes as a key component of post-transplant immunosuppressive therapy, they can also lead to significant side effects and may not always be effective for certain conditions. By considering the unique mechanism and properties of mammalian target of rapamycin (mTOR) inhibitors, such as their anti-inflammatory, anti-fibrotic, and anti-proliferative effects, it appears that they hold great potential in addressing the aforementioned conditions. Despite the potential benefits of mTOR inhibitors, their use in pediatric liver transplant recipients is still controversial and requires careful consideration of the risks and benefits. Moreover, the optimal dosing, timing, and duration of mTOR inhibitor therapy have not been established. In this presentation, the utilization of mTOR inhibitors in pediatric liver transplantation will be reviewed. The focus will be on the evaluation of their impact on various aspects such as renal impairment, acute and chronic rejection, post-transplant lymphoproliferative disease (PTLD), primary malignancies, as well as their side effects. It is hoped that this section will provide additional and comprehensive information on the use of mTOR inhibitors in daily practice for pediatric liver transplant recipients.

KEYWORDS: Pediatrics; Liver transplantation; Calcineurin inhibitors; Mammalian target of rapamycin inhibitors

Induction Therapy in Renal Transplantation: Why? What Age

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ABSTRACT

Induction therapy is immunosuppressive therapy administered at the time of kidney transplantation to reduce the risk of allograft rejection.

All kidney allograft recipients require immunosuppressive therapy to prevent rejection and loss of the allograft. All patients should be immunologically risk assessed before transplantation.

Key reasons for using induction therapy in renal transplantation are: reducing the risk of acute rejection, minimizing the need for high-dose maintenance immunosuppression, enhancing long-term graft survival, Individual patient considerations.

Available antibodies for induction therapy include the following: antilymphocyte antibodies, IL-2 receptor antibody, anti-CD20 monoclonal antibody,

For patients at high immunologic risk of acute rejection (see 'Assessment of immunologic risk' above), we recommend induction therapy with rATG-Thymoglobulin rather than an interleukin (IL) 2 receptor antagonist (basiliximab).

For patients who are at low immunologic risk of acute rejection,either an IL-2 receptor antagonist (basiliximab) or rATG-Thymoglobulin is a reasonable induction therapy agent.

The optimal dosing strategy for rATG-Thymoglobulin is not known, and practice may vary between centers. The optimal cumulative dose for rATG-Thymoglobulin is unknown but is felt to total 3 to 6 mg/kg.

We administer IV basiliximab 20 mg intraoperatively in combination with IV methylprednisolone (7 mg/kg), and 20 mg on postoperative day 4.

KEYWORDS: Induction therapy; ATG; IL-2 antibody

Immunosuppression in Simultaneous Pancreas-kidney Transplantation

Jamshid Roozbeh, MD, Chairman of Executive Committee, IRSOT 2023

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ABSTRACT

Simultaneous pancreas and kidney (SPK) transplantation is indicated for select patients with both type 1 diabetes mellitus (T1DM) and end-stage chronic renal failure. Rejection remains the primary cause of transplant failure following the first months after transplantation.

In the United States, more than 85 percent of pancreas transplants are performed as simultaneous pancreas-kidney (SPK) transplants, with the remainder performed as either sequential pancreas after kidney (PAK) transplants or pancreas transplants alone (PTA). Immunosuppression regimens continue to change over time, with variations from center to center.

INDUCTION THERAPY: Most transplant centers advocate the use of induction therapy for all pancreas Transplants. Available agents for induction include T cell-depleting antibodies (such as polyclonal rabbit anti-thymocyte globulin [rATG]-Thymoglobulin and monoclonal alemtuzumab [anti-CD52 antibody]) and non-depleting antibodies such as interleukin (IL)-2 receptor antibodies (monoclonal basiliximab). Most transplant centers, administer a T cell-depleting agent (either multi-dose rATG-Thymoglobulin or single-dose alemtuzumab) at the time of transplantation. Alemtuzumab and rATG induction were compared in a randomized, single-center trial of kidney and pancreas recipients (222 patients enrolled). Thus, most pancreas transplant centers believe that a greater amount of frontloaded immunosuppression, which is provided by T cell-depleting agents, is warranted in this setting.

MAINTENANCE THERAPY: Following induction with a T cell-depleting agent, we administer maintenance immunosuppression therapy to all SPK. Maintenance therapy is similar for patients receiving an SPK or PAK transplant and typically includes a calcineurin inhibitor, an antimetabolite, and generally a tapering dose of glucocorticoids.

CONCLUSION

Standard immunosuppression entails the use of T cell–depleting agents (commonly anti-thymocyte globulin [ATG]), followed by calcineurin inhibitors (CNIs; mostly tacrolimus [TAC]), an anti-metabolite (mostly mycophenolate mofetil [MMF]) and eventually steroids. Practice may vary from center to center with regards to selection and dosing of a calcineurin inhibitor, anti-metabolite, and glucocorticoids. At some centers, mTOR inhibitors are used either in addition to or in place of any of the above agents. Other centers endorse early glucocorticoid withdrawal or use different glucocorticoid tapering regimens.

KEYWORDS: Simultaneous pancreas and kidney; Induction therapy; Maintenance therapy

Impact of COVID-19 Pandemic on Management of Pediatric Kidney Transplant Recipients

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ABSTRACT

Children appear to be less commonly and less severely affected by COVID-19 than adults, accounting for 1% to 5% of all COVID-19 cases. The COVID-19 pandemic has challenged pediatric kidney transplant programs to provide safe and consistent care during this difficult and unprecedented time. So far during this pandemic, best practices being delivered to pediatric kidney transplant patients are based on available information from published literature and expert opinions. The key areas of pediatric kidney transplant care that may be affected by the COVID-19 pandemic include transplant activity, outpatient clinic activity, monitoring, multidisciplinary care, medications (immunosuppression and others), patient/family education/support, school and employment, and care of pediatric kidney transplant patients who are COVID-19 positive. It has been presumed that children with chronic kidney disease and/or those who take immunosuppressants may be at increased risk for complications from COVID-19 infection; however, available evidence has now suggested that immunosuppressed children with kidney transplant are not at increased risk of severe COVID-19 disease. Clinicians should remain aware that transplant recipients may present with atypical symptoms. In addition, because evidence-based reports to support specific adjustments to immunosuppressive medications in relation to COVID-19 are not yet available, decisions on reduction or discontinuation of immunosuppression should be on a case-by-case basis for kidney transplant recipients who are COVID-19 positive.

CONCLUSION

Reports to support evidence-based management of pediatric kidney transplant patients during the COVID-19 pandemic are lacking; therefore, expert opinion and available knowledge and experience remain subject to biases.

KEYWORDS: COVID-19; Kidney transplantation; Pediatrics

Post-Reperfusion Syndrom in Liver Transplantation

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ABSTRACT

Despite decreasing perioperative mortality seen during OLT in the last 10 years, anesthesiologists and surgical teams continue to encounter major hemodynamic events during the intraoperative period. These have been associated with adverse outcomes during the postoperative period. The overall incidence of PRS varies among reports, ranging somewhere between 8% and 30%. Aggarwal *et al.* defined PRS as a >30% decline in MAP relative to the value before reperfusion during the anhepatic phase that lasts for at least 1 minute, usually occurring within 5 minutes of reperfusion of the donor liver. Hilmi et al. defined significant PRS as a >30% drop in MAP or heart rate, asystole, or hemodynamically significant arrhythmias or the need for continuous infusion of vasopressors during the intraoperative period. Risk factors for PRS are Donor/Organ-related and recipient-related procedure-related. Metabolic acidosis, hyperkalemia. Hypocalcemia, hypothermia, and air emboli are involved in the pathophysiology of PRS. Also, proinflammatory cytokines, and vasoactive agents all have been implicated as likely culprits for PRS. Today, intraoperative increasingly is being used as a valuable diagnostic and monitoring modality in OLT. For prevention and treatment of PRS, hyperkalemia and acidosis should be corrected. Vasopressors, norepinephrine may be preferred over phenylephrine because the latter only influences SVR with no effect on cardiac contractility. vasopressin may be effective in maintaining adequate SVR, even in severe acidosis, when catecholamines such as epinephrine and norepinephrine have proven ineffective. Post-reperfusion vasoplegia that is refractory to vasopressin and catecholamine therapy may be treated with methylene blue (MB). Hydroxocobalamin is a potent scavenger of NO, it may be a suitable alternative for the treatment of PRS owing to vasoplegia, especially when MB is ineffective or contraindicated. Aprotini ameliorates the systemic inflammatory response and release of proinflammatory cytokines that play a significant role in PRS. Plasma magnesium levels decline significantly during the dissection and anhepatic phases of OLT, resulting in hypomagnesemia at the time of reperfusion. Magnesium has been shown to stabilize the cellular transmembrane potential and has immunomodulatory effects. Ischemic preconditioning, through short cycles of reperfusion and ischemia before a prolonged period of ischemia, has been used to protect organs from ischemia-reperfusion injury. However, so far there has been no clinical trial to address the effect of ischemic preconditioning on PRS.

KEYWORDS: Post-reperfusion syndrom; Liver transplantation; Hyperkalemia; Vasopressin

Vaccination after Kidney Transplant

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ABSTRACT

Prevention of infection after kidney transplantation is important and immunization is a way to prevent infection. Although immunocompromised patients are less likely to respond well following vaccination, they should be vaccinated as early in the course of kidney disease as possible to increase the production of protective antibodies. Live attenuated virus vaccines such as Mumps, Rubella, Measles, Varicella, Zoster, and intranasal influenza vaccine should be avoided post-transplantation due to the risk of disseminated diseases. Waiting a minimum of 4 weeks between these vaccines and subsequent transplantation is recommended.

At the post-transplant time, it is common to wait at least 3-12 months for immunization with inactivated vaccines. An exception is for inactivated influenza vaccine that is prescribed as early as one month after transplantation during influenza outbreaks. And then annual administration after transplantation is recommended.

Also avoid vaccination, other than seasonal influenza for six months following treatment for rejection and receiving immunomodulatory treatment (eg, anti-CD20 antibodies, anti-thymocyte globulin).

The American Society of Transplantation (AST) favors the use of the inactivated influenza vaccine for contacts of solid organ transplant recipients; they state that if the live attenuated influenza vaccine is the only available option, it can be given, but vaccine recipients should wash their hands frequently for two weeks following vaccination.

For the pneumococcal vaccine, adult solid organ transplant candidates and recipients should receive either of the following:

1- The 20-valent pneumococcal conjugate vaccine (PCV20) alone or

2- The 15-valent pneumococcal conjugate vaccine (PCV15) followed by the 23-valent polysaccharide pneumococcal vaccine (PPSV23) ≥8 weeks later

Hepatitis B virus vaccination is indicated for all anti-hepatitis B surface antigen (anti-HBs)-negative solid organ transplant candidates. Since a transplant candidate may be offered an organ from an HBsAg-negative, core antibody-positive ("core-positive") donor, or sometimes even an HBsAg-positive donor, the vaccine series should be completed before transplantation if it is possible.

KEYWORDS: Vaccination; Kidney Transplant; Immunocompromised patients

Immunosuppressive Regimen after Lung Transplantation

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ABSTRACT

Lung transplantation can be a life-saving procedure for those with end-stage lung diseases. Unfortunately, long term graft and patient survival are limited by both acute and chronic graft rejection, Immunosuppressive regimens are employed to reduce the rate of rejection. Immunosuppressive regimens included two phases: induction and maintatnce.

Induction therapy is the utilization of a potent immunosuppressive agent in the immediate post-transplant period to reduce the initial robust immune response of T cells to the transplanted organ. Induction agents can be classified into two groups: monoclonal agents, and polyclonal agents (eg anti-thymocyte globulins (ATG) . Overall it appears that induction with either ATG or an IL2 receptor antagonist reduces or delays the incidence of acute rejection, bronchiolitis obliterans syndrome (BOS), and may improve graft and patient survival compared to no induction. Induction with ATG led to improvements in outcomes only in bilateral lung transplant patients when compared to no induction; there were no significant differences in outcomes in single lung transplant recipients receiving ATG versus no induction.

Maintenance immunosuppression usually includes a combination of three drugs: a glucocorticoid (e.g. prednisone), a calcineurin inhibitor (cyclosporine or Tacrolimus), and an anti-metabolite agent (mycophenolate mofetil [MMF] or azathioprine) . For patients receiving the initial dose of TAC sublingually, the usual dose is approximately 0.04 to 0.05 mg/kg/day in two divided doses. Careful monitoring of blood levels is essential. In general, transplant centers aim for a TAC trough target level of 10 to 15 ng/mL for months 1 to 3, 8 to 13 ng/mL for months 4 to 12, and 6 to 8 ng/mL after the first 12 months. If cyclosporine is preferred, the maintenance oral dose is 3 to 5 mg/kg twice a day with Trough levels are targeted at 250 to 350 ng/mL during the initial post-transplant year and 200 to 300 ng/mL subsequently. The dose of MMF is 1000 to 1500 mg orally given twice daily, starting within 72 hours after transplantation.

The usual initial dose of sirolimus is 2 mg per day orally; everolimus is initiated at 1.5 mg twice daily. The therapeutic ranges for sirolimus and everolimus blood levels are 5 to 15 ng/mL and 3 to 12 ng/mL, respectively.

KEYWORDS: Immunosuppressive regimen; Lung transplantation; Induction therapy; Maintenance therapy

No. 2023-1: The Role of moR-US4-1 During Cytomegalovirus Reactivation in Kidney Transplanted Patients

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ABSTRACT

Background: The ability of human cytomegalovirus (HCMV) in reactivation after renal transplantation has been detected as a reason of producing mortality. microRNA offset RNAs (moRNAs, moRs) are regulatory molecules that are originated from the hairpins that are precursors of microRNAs. HCMV genome contains some moRs that might be related with outcome of transplant in the HCMV reactivated kidney transplanted recipients (KTRs). Therefore, in a study, the expression level of moR-US4-1 evaluated in the KTRs with HCMV reactivation.

Methods: Ninety-two people composed of 30 healthy controls and 62 kidney transplanted patients (half of them experienced rejection episodes) were enrolled in the study. An in-house SYBR Green Real-time PCR method was used for evaluation of the moR-US4-1 expression level in different study groups. Additionally, the correlation between expression level of studied moRNAs between patients' groups and also with the level of blood urea nitrogen (BUN) and Creatinine (Cr) were studied. The expression level of tested moRNAs which belongs to the same precursor were compared.

Results: The analyses showed that the expression level of both moR-US4-1-3p/5p were increased in CMV-active KTRs, significantly. Additionally, moR-US4-1-3p had significant correlation with both BUN and Cr level in the CMV-active group of patients. Finally, moR-US4-1-3p/5p showed co-expression pattern in CMV reactivated group of patients, significantly.

Conclusion: The high expression level of moR-US4-1 during CMV reactivation show the importance of these regulatory molecules in studying the outcome of kidney transplantation, therefore, in the future studies more concerns should be paid for such molecules in the context of CMV reactivation.

KEYWORDS: moR-US4-1; Cytomegalovirus; Kidney Transplanted Patients

No. 2023-2: Investigate How Positive Blood Cultures in Deceased Liver Donors Affect Transplant Outcomes and Complications

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ABSTRACT

Background: Liver transplantation is the preferred treatment for end-stage liver disease patients. Due to a shortage of donor organs relative to the population needing liver transplants, many patients die annually while waiting for a transplant. One of the existing concerns is the positive blood culture of brain-dead donors and whether using their organs increases the risk of specific complications, especially infections, in transplant recipients. This study aims to determine the impact of positive blood culture in organ donors (brain-dead individuals) on the outcomes and complications of liver transplantation and the one-year survival rate of both patients and transplanted organs.

Methods: This study conducted a cross-sectional analysis of data recorded in the medical records of liver transplant patients from 1394 to 1396. According to the protocol, individuals with a positive blood culture underwent antibiotic treatment, and if repeat blood cultures were negative within 24 hours, the transplant was performed. If the patient had clinical and laboratory evidence of sepsis, the transplant did not proceed. Liver transplant recipients were divided into two groups based on whether the organ donor's blood culture was positive or negative, and the outcomes of liver transplantation and complications in the two groups were compared.

Results: The study included 18 cases of positive blood cultures and 119 cases of negative blood cultures. This comparison showed no significant relationship between positive blood cultures in the organ donor (brain-dead individual) and the incidence of complications during hospitalization, one-year survival rates, and post-transplant complications.

Conclusion: The results of this study indicate that positive blood cultures in the organ donor do not affect complications during hospitalization, post-transplant complications, and the one-year survival rate of liver transplant patients.

KEYWORDS: Liver transplantation; Positive blood culture; Liver transplant complications

No. 2023-3: Registry of Liver Transplantation at Mashhad University of Medical Sciences

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ABSTRACT

A patient registry is a structured system that utilizes observational study methods to gather clinical or other data to assess specific outcomes for a defined population based on a disease, condition, or exposure. It is also a tool that can be utilized for measuring the impact, effectiveness, and utility of healthcare services and assessing the quality of care.

One of the successful registries at Mashhad University of Medical Sciences is the liver transplant registry, established in 1394. Comprehensive information about liver transplant candidates, including all pre- and post-transplant medical data and intraoperative information, has been recorded in this registry, serving as the foundation for applied and clinical research in this field. The records of all patients who underwent liver transplantation or were listed as liver transplant candidates at Mashhad University of Medical Sciences have been registered. To date, data on 1683 patients have been entered into the registry, of which 551 have undergone liver transplantation. In this context, selecting the Liver Transplant Registry as the top registry in the university's research festival in 1396 and 1401 is a valuable recognition for the university.

The primary objectives of the Liver Transplant Registry include:

- Using data to evaluate and calibrate current prediction models in the Khorasan population.
- Developing predictive models for the survival of liver transplant patients using classical statistical approaches, artificial intelligence, and data mining techniques.
- Discovering hidden relationships among collected variables.
- Identifying factors affecting short- and long-term mortality and morbidity after liver transplantation.
- Identifying factors influencing the mortality of individuals on the liver transplant waiting list.
- Facilitating the implementation of randomized clinical trials, descriptive studies, and retrospective studies.

Today, healthcare systems require accurate, reliable, and comprehensive information for effective management in the healthcare domain. The goal is to achieve the highest results with the least resources, and this objective is attainable through the creation and development of a well-accessible registry.

KEYWORDS: Patient registry; Liver transplant; Prediction model, Healthcare systems

No. 2023-4: Examining the Level of Compliance with the Charter of Patient Rights from the Point of View of Transplant Patients in Mashhad's Montaseriyeh Hospital

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ABSTRACT

Background: Paying attention to patients' rights and respecting them is one of the critical factors for the recovery and comfort of hospitalized patients. The patient's rights have been developed based on the concept of individual and human dignity and equality of all human beings, and it is considered an essential part of health care. In recent years, tremendous progress has been made in organ transplantation, and as a result, the legal and legal issues surrounding it have also become more visible. Therefore, the present study was conducted in order to investigate the level of compliance with the charter of patient's rights from the point of view of transplant patients in Mashhad's Mantasarieh Hospital in 2017.

Methods: The present study is a cross-sectional study that was conducted on all liver and kidney transplant patients during the first 3 months of 2017. In order to measure the level of compliance with the Charter of Patients' Rights, a researcher-made questionnaire was used, which has 28 questions based on the 5 axes of the Charter of Patients' Rights in Iran, with a reliability rate of 80% obtained through Cronbach's alpha. The criterion of compliance with each axis was measured using a Likert scale and the data were analyzed using descriptive tests. This article is the result of a research project with IR.MUMS.FHMPM.REC.1396.358 code of ethics. Sufficient explanations regarding the objectives of the research were given to the subjects and they were assured that all the information collected in this research is confidential.

Results: Most of the patients were in the age group of 30 to 40 years. Out of 60.6% of male patients and 39.4% of female patients, 74.7% lived in the city and 25.3% lived in the village. 40.9% of the patients had a diploma. The transplanted organ was in 67.7% of kidney and 22.2% of liver patients. Examining the main axes of the charter of patient rights showed that the first to fifth axes have been observed by 80.27, 60.08, 47.9, 62.02, and 49.5 percent, respectively.

Conclusion: The results of the present study showed that the right of "optimal receipt of health services" was well respected, but the right of "the patient's right to freely choose and decide to receive health services" was not well respected. Since some patients were not placed in situations related to the charter of patient rights; It is suggested to compile a special charter for transplant patients and the care team members should pay more attention to the special condition of these patients. At the same time, this leads to an increase in the satisfaction of transplant patients.

KEYWORDS: Patient rights; Transplant patients; Kidney transplant; Liver transplant

No. 2023-5: Evaluation of Clinicopathologic Characteristics of Bile Ducts in Post-liver Transplant Patients with Biliary Stricture in Abu-Ali Sina Hospitals for Five Years

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ABSTRACT

Background: Biliary strictures are one of the most common complications following liver transplantation, representing an important cause of morbidity and mortality in transplant recipients. The reported incidence of biliary stricture is 5% to 15% following deceased donor liver transplantations and 28% to 32% following living donor liver transplantations. We aim to evaluate the clinical and pathological characteristics of patients with post-transplant biliary stricture that underwent resection of stricture site.

Methods: This is a retrospective cross-sectional study, the pathology files of Namazi and Abualisina Hospitals lab from 1388 till 1400 were evaluated. After selection of patients, the pathology slides were extracted from pathology file and reviewed by an expert pathologist and the histopathological findings were collected in predesigned forms. The histopathological findings consisted of fibrosis, epithelial injury, neuroma, tumor, and other related findings. The demographic and clinical data were also extracted from the patient's clinical file.

Results: During the period of our study, a total of 48 patients were included. The age of the participants ranged from one year to 65 years old, with an average of 44.25 ±16.34 years. Among the patients, 33 (68.8%) were male while 15 (31.3%) were female. The most frequent etiology in our study was cryptogenic liver disease (20.8%), and the most common sign was the rise of LFT (77.8%). Also, 7 (14.6%) of the patients underwent PTBD and the mortality rate in our study was 18.8%. Also, one of the cases had fungal elements. Traumatic neuroma was observed in 14 (29.2%) of patients. Direct bilirubin and the direct to total bilirubin ratio were significantly lower among the traumatic neuroma cases. Patients with traumatic neuroma had significantly lower rates of chronic inflammation (P=0.036) and higher rates of nerve hyperplasia. (P=0.021).

Conclusion: Due to the rise in liver transplantation around the world prevalence of biliary complication has increased. We observed an incidence of 29.2% traumatic neuroma among our cohort of 48 patients with biliary complications. Physicians are urged to remain mindful of malignant biliary strictures as they may easily mimic and misguide the diagnosis of a traumatic biliary neuroma.

KEYWORDS: Cirrhosis; Liver transplant; Pathology; Biliary Stricture

No. 2023-6: Outcome of Haploidentical versus Matched Sibling Donors in Hematopoietic Stem Cell Transplantation for Adult Patients with Acute Lymphoblastic Leukemia: A Study from the Acute Leukemia Working Party of the Iranian Society for Blood and Marrow Transplantation

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ABSTRACT

Background: Non-T-cell depleted haploidentical hematopoietic stem cell transplantation (HaploSCT) is being increasingly used in acute lymphoblastic leukemia (ALL) with improving patient outcomes. We have recently reported that outcomes of adult patients (pts) with ALL in complete remission (CR) receiving HaploSCT are comparable to unrelated donor transplants. We now compared HaploSCT and matched sibling donor (MSD) transplants in pts with ALL. To assess transplantation outcomes of HaploSCT and MSD transplants in pts with ALL in CR.

Methods: We retrospectively analyzed adult patients (≥ 18 years) with ALL who underwent their first allogeneic stem cell transplantation (alloSCT) in first or second CR between 2015 and 21 either from a T cell replete Haplo or MSD donor, and whose data were reported to the Acute Leukemia Working Party (ALWP) of the European Society for Blood and Marrow Transplantation (EBMT). Multivariate analysis (MVA) adjusting for differences between the groups was performed using the Cox proportional hazards regression model. Propensity score matching was also performed to reduce confounding effects.

Results: The analysis comprised 2500 patients: HaploSCT-413; MSD-1845. Median follow-up was 25 months. Median age was 37 (range 18–77) and 38 (18–77) years in HaploSCT and MSD, respectively. HaploSCT patients were transplanted more recently than those transplanted from MSD (2016 vs 2015, $p < 0.0001$). A higher rate of HaploSCT was in CR2 (33.4% vs 16.7%, $p < 0.0001$), respectively, and fewer received myeloablative conditioning (68% vs 85.2%, $p < 0.0001$). Cytomegalovirus (CMV) seropositivity was lower in HaploSCT patients (22% vs 28%, $p = 0.01$) and donors (25.1% vs 33%, $p < 0.02$), and a higher proportion of the HaploSCTs were performed using a bone marrow (BM) graft (46.2% vs 18.6%, $p < 0.0001$). The 2 groups did not differ with regard to gender, Karnofsky performance status score, ALL phenotype, Philadelphia chromosome (Ph) positivity and pre-alloSCT measurable residual disease (MRD). Graft versus host disease (GVHD) prophylaxis was mainly post-transplant cyclophosphamide (PTCy) based (92.7%) in the HaploSCT setting, while it was mostly pharmacologic in the setting of MSD (18.7% received ATG). Cumulative incidence of engraftment at day 60 was higher in MSD transplants compared to HaploSCT (98.7% vs 96.3%, $p = 0.001$), respectively. Day 180 incidence of acute (a) GVHD II-IV and III-IV was higher in HaploSCT vs. MSD: 36.3% vs 25.9% ($p = 0.002$ and 15.2% vs 10.5% ($p = 0.005$), respectively. Conversely, the 2-year chronic (c) GVHD and extensive cGVHD were 32% vs 38.8% ($p = 0.009$) and 11.9% vs 19.5% ($p = 0.001$) in HaploSCT vs MSD, respectively. Main causes of death were leukemia (31.8% vs 45%), infection (33.1% vs 21.7%) and GVHD (16.6% vs 19.7%) for HaploSCT and MSD, respectively. Two-year relapse incidence (RI),

non-relapse mortality (NRM), leukemia-free survival (LFS), overall survival (OS) and GVHD-free, relapse-free survival (GRFS) were 26% vs 31.6%, 22.9% vs 13%, 51% vs 55.4%, 58.8% vs 67.4% and 40.6% vs 39% for HaploSCT and MSD, respectively. In the MVA, RI was significantly lower in HaploSCT in comparison with MSD, hazard ratio (HR) = 0.66 (95% CI 0.52–0.83, p = 0.004), while NRM was significantly higher, HR = 1.9 (95% CI 1.43–2.53, p < 0.0001). aGVHD grade II-IV and grade III-IV were higher in HaploSCT than in MSD HR = 1.55 (95% CI 1.23–1.9, p = 0.0002) and HR = 1.54 (95% CI 1.1–2.15, p = 0.011), respectively. Extensive cGVHD was lower in HaploSCT compared with MSD, HR = 0.61 (95% CI 0.43–0.88, p = 0.6, while total cGVHD did not differ significantly, HR = 0.94 (95% CI 0.74–1.18, p = 0.58). LFS, OS and GRFS did not differ significantly between the 2 transplant groups, HR = 0.96 (95% CI 0.81–1.14, p = 0.66); HR = 1.18 (95% CI 0.96–1.43, p = 0.11) and HR = 0.93 (95% CI 0.77–1.09, p = 0.35), respectively. These results were confirmed in a matched-pair analysis.

Conclusion: Outcomes of adult patients with ALL in CR receiving alloSCT from haploidentical donors are not significantly different from those receiving transplants from MSD in terms of LFS, OS and GRFS. .

KEYWORDS: Allogeneic stem cell transplantation; Acute lymphoblastic leukemia; Haploidentical; Sibling; Donor

No. 2023-7: The relationship between Weight Indices and Blood Levels of Immunosuppressive Drugs in Renal Transplant Recipients

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ABSTRACT

Background: Calcineurin and mTOR (mammalian target of rapamycin) inhibitor drugs are crucial for maintaining the transplanted organ, however, net body weight may not be a good measure to determine these medications' dose or predict their blood concentration. There is some contradiction in the results of previous studies, regarding the effect of obesity on the blood concentration of these drugs or the success of transplantation, therefore, this study aimed to evaluate a variety of weight indices to identify an indicator of weight that has the best relationship with the blood level of drugs used in organ transplantation.

Methods: This was a retrospective descriptive-analytical study. Participants were selected from the patients referred to the nephrology clinics affiliated with Isfahan University of Medical Sciences who were consuming one of the calcineurin and/or mTOR inhibitor drugs. The information needed to achieve the project's goals was extracted from the patient's medical records. These include demographic and clinical data, namely height, weight, and all weight indices (total/ideal/adjusted body weight, lean body man, body mass index, and predicted normal weight), as well as blood levels of immunosuppressive drugs, in every patient's visit. Regarding the dosage (based on mg/kg) of each administered drug, the gathered data were analyzed to find out the weight indices which correlate the best with obtained blood concentration of each immunosuppressive drug. This research uses the GEE (generalized estimating equation) model with logistic regression, independent correlation matrix, and binary distribution for data analysis.

Results: In this study, the medical records of 127 patients were examined, all of whom have more than three visit sessions with complete information in the medical file. Their information, which included a total of 1337 visit sessions, was collected, recorded, and analyzed. In this study, trough (C0) concentrations of drugs were collected based on the laboratory data of each patient, then the C0 concentration was analyzed in relation to each weight index (as an indicator) and the resulting number was used as an odd's ratio (OR) for statistical comparison. For cyclosporine, tacrolimus, and sirolimus, all the indicators have increased the chance of creating the appropriate concentration, while drug dosing based on the lean body mass (OR: 1.028), the ideal body weight (OR: 1.075), and the total body weight (OR: 1.041) have the best relationship with proper cyclosporine, tacrolimus, and sirolimus blood levels, respectively.

Conclusion: Using all of the indicators for calculating the proper dose (as mg/kg) of each mentioned immunosuppressive drug for an individualized patient, has increased the chance of creating the appropriate blood concentration of the drug, while this ratio is different for each medication by applying any of introduced weight indices. This can be more evident by performing studies based on TDM (therapeutic drug monitoring) plans in transplant centers.

KEYWORDS: Calcineurin inhibitors; mTOR inhibitors; Weight indices; Immunosuppressive drugs; Transplantation

No. 2023-8: The Outcomes of Cochlear Implantation in Solid Organ Transplanted Patients

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ABSTRACT

Background: As far as it is known, long-lasting immunosuppressive therapy might prone patients with solid organ transplantation (SOT) at increased risk for severe to profound sensorineural hearing loss, eventually leading to cochlear implantation (C.I). So, the main aim of the present study is to evaluate their auditory perception performance after cochlear implantation.

Methods: This case-series study assessed the auditory perception performance of our center's six cochlear implanted patients who had undergone solid organ transplantation before. The patients' age range was between 3 to 68 years old. Two participants (Female/ male) had received liver transplantation and the rest (2 males, 2 females) had undergone kidney transplantation. The assessment was conducted through the CAP (Categories of Auditory Performance) test in the first month of cochlear implantation and 12 months later.

Results: Except for one patient (A 3 years old girl) who has recently received a cochlear implantation device, and her rehabilitation program is in progress, the auditory perception performance of others improved from 2 to at least six scores. Also, no wound infection, mastoiditis, or bacterial meningitis occurred after cochlear implantation.

Conclusion: Immunosuppressive therapy, hemodialysis, infections, and long-lasting medication might lead to severe to profound sensory neural hearing loss in organ-transplanted patients. In recent years, cochlear implantation has been considered a final solution to help this group of patients to hear and communicate better.

KEYWORDS: Solid organ transplantation; Cochlear implantation; Immunosuppressive therapy

No. 2023-9: Trientine as an Ominous Agent behind Morbilliform Eruptions in Wilson Disease: Lessons from a Case Study

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ABSTRACT

Morbilliform eruptions are serious cutaneous manifestations with various etiologies. Although, its pathophysiology is partially understood, its etiology remained unclear. Drug-induced eruptions and infectious diseases remain as the leading etiologies in differential diagnoses. Trientine in this case resulted in a drug-induced allergic maculopapular rash, a very rare side effect of trientine. Rashes occurred on the skin fold area. Due to the rarity of this side effect, there is no practical guideline to handle this condition, case studies are important to recommend a therapeutic option. Herein, at first, Trientine was discontinued and short-term Corticosteroid therapy started beside Zinc monotherapy, which was replaced as an effective alternative drug in WD patients experiencing side effects from chelation therapy.

KEYWORDS: Trientine; Morbilliform Eruptions; Wilson Disease

No. 2023-10: Kidney Transplantation and Immunosuppressive Agents

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ABSTRACT

Immunosuppressive drugs have made kidney transplantation the optimal treatment for patients with end-stage renal disease. The reduction of acute transplant rejection by current therapies and most potential new drugs has led to the survival of kidney transplants and improved patient and allograft outcomes. T-cell depleting agents apply for induction and maintenance immunosuppression in adult kidney transplant recipients. Calcineurin inhibitors (CNIs), azathioprine, mycophenolate mofetil (MPA), belatacept, steroids, and mammalian target of rapamycin (mTOR) inhibitors are all maintenance immunosuppressive agents. CNIs bind to their binding proteins and prevent the release of calcineurin and IL-2 transcription. Azathioprine inhibits DNA synthesis, and MPA inhibits Inosine-5′- monophosphate dehydrogenase and prevents purine synthesis. Belatacept blocks CD80/86 - CD28 co-stimulation, and steroids inhibit the transcription of inflammatory cytokines. mTOR inhibitors restrain signal transduction through mTOR and stop the cell cycle. CNIs have obviously impacted allograft outcomes, mainly used in combination with azathioprine or MPA. Randomized controlled trials showed higher graft survival and better allograft outcomes for treatment with tacrolimus than cyclosporine and MPA compared to azathioprine with or without prednisone in recipients.

Standard immunosuppression with T-cell depleting therapy and tacrolimus- MPA-based maintenance has stayed the most widely used regimen for years as the "gold standard". On the other hand, the wide range of side effects related to immunosuppressive drugs creates an opportunity for emerging treatments.

This review summarizes individual agents and multidrug regimens for current treatment standards for kidney recipients and discusses novel therapies.

KEYWORDS: Azathioprine; Calcineurin inhibitor; Immunosuppression; Kidney transplant; mTOR inhibitors; Mycophenolate mofetil; Steroids

No. 2023-11: Cell Encapsulation; A Way for Cell Transplantation

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ABSTRACT

Cell-based therapy is emerging as a promising strategy for the treatment of a wide range of human diseases such as diabetes, blood disorders, acute liver failure, spinal cord injury and several types of cancer. Pancreatic islets, blood cells, liver cells, and stem cells are among the cell types currently used for this strategy. Stem cells can be considered a treatment for people with cancers such as leukemia and lymphoma. This method is also used for multiple myeloma and neuroblastoma and is being investigated as a treatment for other cancers as well. One very common area in nanobiology is improving living cells by capsulation them with monolayers that allow them to acquire these structural and functional properties. Encapsulating the "therapeutic" cells not only prevents immune system rejection, but also provides a controlled and supportive environment in which they can function effectively. The characteristics of cell encapsulation allow this biotechnology to be used for drug delivery or cell delivery. In cell encapsulation technology, encapsulated cells act as factories synthesizing desired therapeutic molecules. Looking to the future, cell therapy is expected to progress significantly by encapsulating cells inside semi-permeable polymers. The inherent potential and effectiveness of this technique in the field of cell confinement will increase dramatically with the development of tissue engineering and regenerative medicine.

KEYWORDS: Natural killer cells; Rejection; Transplantation

No. 2023-12: Cell Sheet Engineering for Liver Transplantation

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ABSTRACT

The liver plays a vital role in metabolism, maintenance of homeostasis, food synthesis and storage, detoxification and defense against microorganisms. The increasing number of liver diseases in the world and Iran, the need to carry out research and it has doubled the invention of new treatment methods. Liver transplantation has been considered a unique treatment method for the treatment of acute and chronic liver diseases, but due to the lack of donor organs, suppression of the recipient's immune system, the invasiveness of the procedure, the complexity of the surgery, and high costs, transplantation Liver is not a good solution for treating diseases. In recent years, cell transplantation and methods based on cell therapy have been proposed as an alternative and modern method for treating liver diseases. Tissue engineering and cell sheet technique is an alternative and promising method for liver regeneration and orthotopic liver transplantation. Sheets of Cells are created by growing on polymer or using the magnetic field property of magnetite nanoparticles to maintain the connections and adhesion of cells. Cultured cells synthesize and secrete their own ECM and stimulate cell sheets to produce them. Cell sheets surrounded by ECM are able to integrate with host tissues, which accelerate liver function after tissue transplantation and are used as tissue engineering without the intervention of scaffolds.

KEYWORDS: Liver; Transplantation; Cell Sheet Technology; Tissue Engineering

No. 2023-13: COVID-19 Outcomes in Kidney Transplant Recipients: A Two-Center Cohort Study from March 2020 to October 2021

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ABSTRACT

Background: COVID-19 is one the very dangerous contagious diseases and the aim of this study was to evaluate the prevalence and outcome of it in hospitalized patients with kidney transplantation in Imam Khomeini and Taleghani hospitals, Urmia, from March 2020 to September 2021.

Methods: We reviewed the medical records of 38 confirmed COVID-19 deceased cases hospitalized in 2 hospitals. Patients' demographics and clinical data, disease severity and adverse outcomes such as intensive care unit admission, mechanical ventilation, and mortality as well as medications prescribed to patients were extracted. Descriptive analysis, analysis of variance, Fisher exact test and multivariate analysis were conducted for data analysis.

Results: The 38 patients met inclusion criteria, and 21 patients (55.3%) were male. the mean age and length of hospital stay (LOS) were 51.26 (±14.22) years (range28 to 87) and 6.55±3.68 days (range1 to 20). The severity of disease was severe in 36.84% (n=`4). Hypertension (HTN) and Diabetes mellitus were two highest reported co-morbidities (60.53% and 31.58% respectively). Continuation of immunosuppression treatment in patients during hospital stay, did not imposing to death and influence treatment outcomes. Although, the mean of duration of intubation and ICU/hospital stay in patients who received cyclosporine or mycophenolate or concomitantly use during hospitalization, were lower than non-continuous group (not significant). Patients with more than 3 presenting symptoms (20 subjects) in compare to subjects with 3 ones and less (18 subjects), had longer hospital stay, duration of ICU admission and tracheal intubation but not significantly. Fever, Shortness of breath, and Myalgia were the most common clinical symptoms; As well as, mortality rate and ICU admission were higher in patients with 3 or more symptoms with P value of 0.06 and 0.39 respectively.

Conclusion: The findings underscored the importance of number of symptoms during hospitalization, time to start covid-therapy, and received immunosuppressant agents in patients with kidney transplantation resulted to increase length of hospital stay. Its recommended to close monitoring of this population in unknown viral disease due to higher risk of mortality.

KEYWORDS: COVID-19; Clinical outcome; Kidney transplant; Immunosuppression

No. 2023-14: Unexpected Hyperphosphatemia and Delayed Graft Function: A Case Report and Literature

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ABSTRACT

Background: Parathyroidectomy (PTX) remains a preferable treatment for dialysis patients with refractory secondary hyperparathyroidism. The main goal of this surgical treatment is maintaining an adequate balance between the prevention of persistent/recurrent disease and avoidance of postoperative hyperparathyroidism. Parathyroid insufficiency occurs infrequently after PTX. Owing to the presence of supernumerary and other glands in the thymus, total suppression of PTH is uncommon even after total PTX without immediate autotransplantation (AT). It seems that constant motivation of elevated phosphorus and decreased 1,25 dihydroxy vitamin D level on isolated cell nests in the thyroid glands, thymus, and cervical fat, account for detectable PTH after total PTX in end-stage renal disease (ESRD) patients. However, in patients with a history of total PTX undergoing successful kidney transplantation, constant stimulation of cell nests is no longer expected due to the well-functioning of the allograft. Unexpectedly, this drop in PTH values through the first postoperative week in kidney-transplanted patients could result in considerable hyperphosphatemia. Production of calcium phosphate particles in the renal luminal tube, could initiate interstitial inflammation, activation of toll-like receptor 4, and finally development of renal damage as named acute phosphate nephropathy (APN). Subtotal parathyroidectomy which involves the resection of three and a half parathyroid glands is considered a better treatment choice for ESRD patients awaiting allograft.

Case Report: In this study, we described a 35 years old male ESRD patient with a history of total parathyroidectomy that 4 months later received a kidney allograft. The function of the graft remained stable for one week. After that, creatinine levels gradually decreased, and spontaneously the mean of calcium received to 5.6 mg/dl and the mean of phosphorus received to 6.7 mg/dl. It was observed that the function of the graft drastically decreased and after the prescribing recombinant PTH, all of these parameters were normalized and the graft function was stabilized.

Conclusion: APN should be considered in kidney transplanted patients with a history of total PTX and acute onset of allograft failure without a well-known reason.

KEYWORDS: Total parathyroidectomy; Hyperparathyroidism; Kidney transplantation

No. 2023-15: Uncommon Chronic Kidney Diseases after Kidney Transplantation

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ABSTRACT

Background: Kidney transplantation is the best applicable procedure for patients with end-stage renal disease (ESRD); however, the prevalence of uncommon chronic kidney diseases (CKDs) is growing up after transplantation. Some uncommon CKDs include adenine phosphoribosyl transferase (APRT) deficiency, primary hyperoxaluria (PH), fibrillary glomerulonephritis (FGN), and C3 glomerulopathy (C3 GP).

Results: APRT deficiency is generated from mutations in the APRT gene that result in the complete reduction of the ARPT enzyme. PH occurs by the absence of liver alanine glyoxylate aminotransferase that normally converts glyoxylate to glycine. Aggregated C3 resulted from the deregulation of alternative complement pathways and the absence of immunoglobulin in glomeruli leads to C3 GP. FGN as another rare glomerular disease is defined by the presence of fibrils in the glomeruli.

Conclusion: It seems that monitoring uncommon CKD diseases among graft candidates with a history of bilateral nephrocalcinosis or nephrolithiasis before kidney transplantation is essential.

KEYWORDS: Chronic kidney disease; Kidney transplantation; Primary hyperoxaluria; Adenine phosphoribosyl transferase; C3 glomerulopathy; Fibrillary glomerulonephritis

No. 2023-16: Hepatitis B Virus Reactivation Due to Bone Marrow Transplant; An Overview on Prophylactic Drugs

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ABSTRACT

Background: Reactivation of hepatitis B virus in people with chronic hepatitis infection can be one of the consequences of bone marrow transplantation or chemotherapy in cancer patients, which worsens the conditions of transplantation. Reactivation of the virus, leading to increased replication, occurs as a result of immunosuppressive regimens used after chemotherapy or bone marrow transplantation. In the meantime, by stopping the use of immunosuppressive drugs and rebuilding the immune system, the attack of immune agents on cells infected with the virus can lead to severe liver damage and the occurrence of clinical symptoms related to it, which may sometimes lead to death.

Results: To avoid this problem, some antiviral drugs such as famciclovir and lamivudine are recommended, which are nucleoside analogues. These drugs stop or disrupt the replication cycle of the virus and prevent its reactivation. The prophylactic use of such drugs is recommended by starting immunosuppressive drugs or starting chemotherapy in cancer patients who are infected with HBV, but so far There is no consensus on the dosage or the time to stop using these drugs.

Conclusion: In this article, we will review some of the past studies that have aimed to prevent HBV reactivation by using prophylactic antiviral drugs; And we will review the treatment method, type and dosage of the drugs suggested in each. It should be noted that early discontinuation of antiviral drugs can lead to reactivation of the virus. On the other hand, long-term use of these drugs as prophylaxis may also cause resistance in mutated and new strains of the virus. Therefore, it is very important to accurately diagnose chronic HBV infection in patients who intend to receive a bone marrow transplant or undergo chemotherapy, and the timely use of antiviral drugs, considering the type and effective dose of them.

KEYWORDS: Bone marrow transplantation; HBV-reactivation; Prophylactic drugs

No. 2023-17: Kidney and Urinary Tract Problems in Pediatric Anorectal Malformations

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ABSTRACT

Background: Anorectal malformations (ARMs) can occur in isolation or in association with other anomalies, most commonly those of the genitourinary systems, and may result in upper urinary tract deterioration. We aimed to analyze the frequency, clinical course, and management of children with children with ARM.

Methods: This cross-sectional study was evaluated infants and children with ARM who received surgery and were followed at the Dr. Shaikh Children's Hospital, Mashhad, IRAN, from 2000 to 2022.

Results: Four hundred and fifty-five children with anorectal malformations were studied, after excluding 55 children with incomplete data. The series included 237 boys and 218 girls with low (153), intermediate (52) and high (250) imperforate anus. The overall incidence of urological anomalies was 47.2%. The most common anomalies were vesicoureteral reflux (VUR), single kidney, ectopic kidney and neurogenic bladder, in order of frequency. End stage kidney disease (ESRD) was noted in 8.7%, in children who had recurrent urinary tract infections, neurogenic bladder or complex renal tract pathology. The incidence of urologic anomalies was significantly higher in children with high imperforate anus in compare with others.

Conclusion: Urological anomalies were seen in 47.2% of patients, but the overall incidence of end-stage renal disease is low. Ultrasonography of the urinary tract should be performed in all children with AMR at the infancy age. Voiding cysto-urethrography can be reserved for patients with dilated upper urinary tracts, urinary tract infections or lumbosacral and spinal abnormalities. Early identification of infants with ARM at risk of renal failure may be important for renal survival.

KEYWORDS: Anorectal malformation; Children; Kidney and urinary tract anomalies; End-stage kidney disease

No. 2023-18: Dynamic Shifts in Brain Death Etiologies: A Comprehensive Study of the Donors Over a Decade

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ABSTRACT

Background: Organ transplantation is often considered the last treatment option for end-stage diseases. While organs can be obtained from living and cardiac dead donors, a significant majority of donations come from brain-dead donors, both globally and in Iran. This underscores the importance of focusing on brain-dead cases, improving the detection, and providing optimal care to preserve organs. While trauma was traditionally the leading cause of brain death in Iran, recent observations have shown a shift in this matter.

Methods: To assess changes in the causes of brain death, we collected data on brain-dead donors who underwent organ recovery at our organ procurement center from January 2007 to December 2022. To facilitate analysis, we divided this data into four 4-year periods: 2007-2010, 2011-2014, 2015-2018, and 2019-2022. Then, we compared the etiologies of brain death across these periods using Additionally, we compared this pattern between the first and second 8-year periods.

Results: Demographic characteristics of the brain-dead donors is depicted in Table 1. During the study period (2007-2022), 2,269 donors underwent organ recovery at our center. Evaluation of six different causes of brain death occurrence, including trauma, cerebrovascular accidents, brain tumors, hypoxia, non-traumatic cranial bleeding, and toxicity, revealed varying patterns in each time period. Statistical analysis confirmed the significance of these alterations ($P< 0.001$). The most prevalent cause of brain death in both 1st and 2nd periods was trauma, followed by non-traumatic cranial bleeding . Notably, the rate of brain death due to trauma decreased (1^{st}: 55.8%, 2^{nd}: 34.2%, 3^{rd}: 24.1%, 4^{th}: 20.1%), while non-traumatic cranial bleeding increased (1^{st}: 15.5%, 2^{nd}: 22.0%, 3^{rd}: 37.3%, 4^{th}: 40.1%) (Fig. 1).

Conclusion: Understanding the etiology of brain death is crucial, as it serves as the primary source of donated organs. Our evaluation revealed that non-traumatic cranial bleeding has surpassed trauma as the leading cause of brain death. Several factors may contribute to this shift, such as improved road safety measures and public awareness of seatbelt use. However, the exact reasons behind this change remain unclear, warranting further investigation.

KEYWORDS: Donors; Organ donation; Brain death; Dynamic Shifts; Etiologies

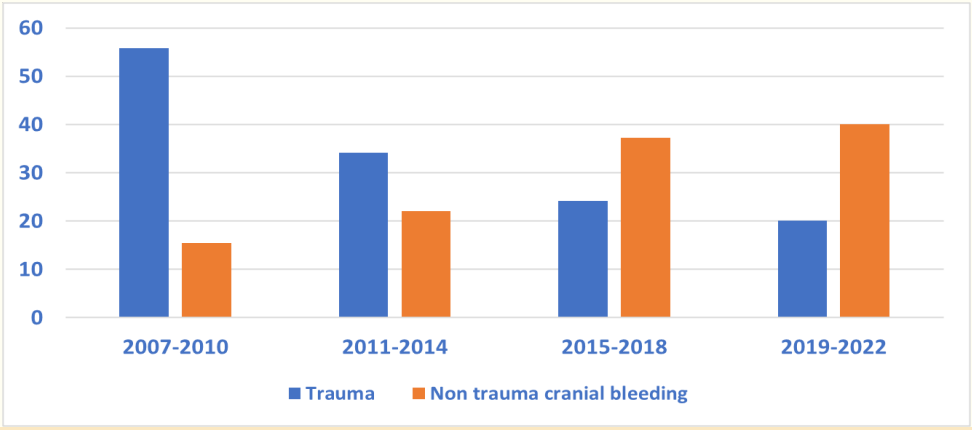

Figure 1: The frequency of trauma and non-trauma cranial bleeding of brain dead organ donors.

Table 1: Demographic characteristics of the brain-dead donors.

Item	2007-2010	2011-2014	2015-2018	2019-2022
Gender (male %)	64	63	67	61
Mean Age (years)	32.5 ± 16.27	38.1 ± 17.48	36.1 ± 18.48	41 ± 13.12

No. 2023-19: The Trend of Family Refusal Causes for Organ Donation: A preliminary Study

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ABSTRACT

Background: Now, solid organ transplantation is a promising therapeutic method for life-saving in organ failure. The main source of procuring organs for transplantation is brain-dead cases. However, organ shortage is a concern among medical staff involving organ transplantation. Family refusal is an important cause of the low conversion rate of possible donors to actual donors. Many attempts have occurred to improve the knowledge of society regarding brain death. We aimed to compare the etiologies of family refusal during 17 years of our experiences.

Methods: We assessed the trend of causes of family refusal in three time points including 2009, 2016, and 2022. The families were interviewed using a semi-structured questionnaire and were asked about the main cause of their decision.

Results: The family consent rate was 80%, 84.4%, and 78% in 209, 2016 and 2022. Brain death denial reduced significantly from 44.4% in 2009 to 12.7% in 2016 and reached 23.3% in 2022. Unawareness about the potential donor wishes was the new concern in 2022 with a dramatic rise (9.2%). The expectation of miracles and promising technologies for the life-saving of a brain-dead body were the other causes that involved our coordinators with a frequency of 13.6% in 2009, 10.9% in 2016, and 25% in 2022 (Fig 1). “Being judged by other people" were the cause of family refusal in 11.5% of the families while this item was highlighted in less than 4 % in 2009 and 2016. Moreover, a guilty conscience resulted in the family refusing in pediatric age group.

Conclusion: In 2022, COVID 19 affected organ donation, however, considering about 2 decades of activity in the field of increasing people's awareness in creating positive attitudes regarding organ donation in society, it seems that both believing in the occurrence of miracles and being judged by others are still some challenges for families to make decisions. The fact that sometimes false content is prepared with the theme of organ donation and is easily published via virtual media in society also easily harms this issue. On the other hand, organ donation advertisements should be done carefully so that the viewer of these advertisements doesn’t declare unwillingness to donate organs in case of brain death situation. Organ donation from brain-dead people is a complex phenomenon with social, moral, and religious dimensions. Hence, it is crucial to pay attention to all dimensions to increase the rate of consent to donation.

KEYWORDS: Hospital; Organ donation; Family consent; Family refusal; Brain death

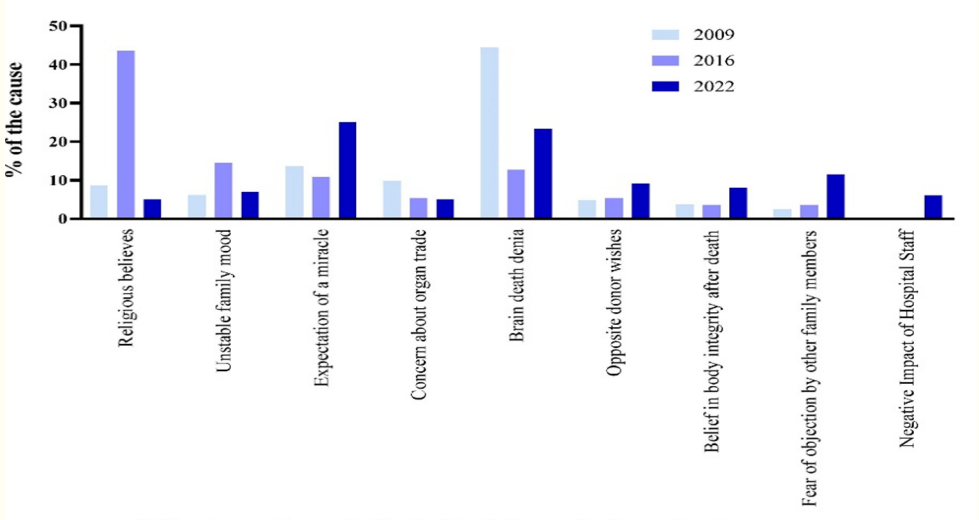

Figure 1: Different causes of family refusal in 2009, 2016, 2022.

No. 2023-20: Toxicity and Poisoning-Related Brain Death: A Critical Risk Factor for Pre-Recovery Cardiac Death in Donors

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ABSTRACT

Background: Organ transplantation represents the last treatment option for patients who suffered from end-stage organ diseases. Unfortunately, the shortage of organ donors and donated organs presents a significant barrier to meeting the needs of patients requiring transplants. Therefore, enhancing organ donation rates is of paramount importance. Organ procurement is feasible from various sources, including brain-dead donors, cardiac-dead donors, and living donors. Globally, the majority of organ donors are brain-dead donors, emphasizing the need to optimize the entire process of donation from brain dead patients that is donor identification to organ preservation. In this study, we aimed to assess the incidence of pre-recovery cardiac death in potential donors and its association with the underlying causes of brain death.

Methods: Utilization rate is a measure of how efficiently donors are being used in transplantation. It is calculated by dividing the number of utilized donors by the total number of actual donors. However, cardiac death in potential organ donors prior to organ recovery due to hemodynamic and physiological alterations triggered by brain death leads to donor loss. We compiled data on actual donors transferred to our organ procurement center over a 17-year period, dating back to 2006. We examined the occurrence of pre-recovery cardiac death in these cases and investigated the brain death etiologies, exploring potential associations between the cause of brain death and the incidence of cardiac death. Our analysis relied on the Chi-square analysis method, and we also assessed the impact of each specific cause of death on pre-recovery cardiac death individually.

Results: In our OPU, utilization rate was 93% in 2022 that irreversible cardiac death was the responsible of a small proportion of it. Among 2,114 cases of brain death who were transferred to our center, 42 cases (2.0%) experienced cardiac death prior to recovery. The incidence rates based on brain death etiology were as the table shows. Statistical analysis of pre-recovery cardiac death rates showed a significant variation based on the cause of brain death (P-Value: 0.37). For a more detailed evaluation, we analyzed each etiology separately and compared the incidence rates of cardiac death between the studied cause and all other causes combined. This

analysis revealed a roughly three-fold higher risk of cardiac death in potential donors who died from toxicity and poisoning (5.3%) compared to those with all other causes (1.7%). Statistical analysis confirmed the significance of this higher rate (P-Value : 0.004, CI: 1.23 – 1.63, OR1.49).

Conclusion: Given the significant shortage of organs available for transplantation, preserving potential organ donors is a life-saving imperative. Therefore, it is crucial to understand the risk factors that increase the likelihood of cardiac death in potential organ donors and take measures to reduce these risks while improving the management of at-risk potential donors. Our investigation underscores the heightened risk of cardiac death associated with brain death due to toxicity and poisoning, emphasizing the need for caution when dealing with potential donors in this group.

KEYWORDS: Donors; Organ donation; Brain death; Cardiac Death; Toxicity

Table 1: The frequency of cardiac death.

Toxicity and poisoning	Brain tumor	Cerebrovascular accident	Trauma	non-traumatic cranial bleeding	Hypoxia
5.3% (7 cases)	3.5% (4 cases)	2.8% (7 cases)	1.3% (12 cases)	1.6% (9cases)	1.4% (3cases)

No. 2023-21: Stem Cell Therapy in Kidney Transplantation

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ABSTRACT

Nowadays, kidney transplantation (KT) is the gold standard strategy for treating patients with end-stage renal disease (ESRD). Despite progressive advances in immunosuppressive drugs, surgical techniques, organ preservation, and intensive care, post-transplant complications, long-term allograft survival and life span have not improved significantly.

Mesenchymal stem cells (MSCs), as non-hematopoietic multipotent stem cells, can be originated from bone marrow, adipose tissue, cord cells, amniotic fluid, and molar cells. International society of cellular therapy (ISCT) indicated that CD105, CD90, and CD73 as stromal cell markers (not hematopoietic markers including CD45, CD34, and CD14) are expressed in MSCs. In recent years, it was shown that MSC therapy could be applied to different immunological disorders like cancers, multiple sclerosis (MS), diabetes, rheumatoid arthritis (RA), and Crohn's disease along with solid organ transplantation.

Human MSCs are capable to inhibit allograft recognition, produce cytokines by interfering with the actions of T-lymphocytes and dendritic cells, and release immunomodulatory cytokines by providing a local immunosuppressive microenvironment. Beyond decreasing the cellular- and antibody-mediated rejection episodes, MSCs present anti-oxidative, pro-angiogenic, anti-apoptotic, and tolerogenic properties that make them the candidate therapy for managing ischemia-reperfusion injury, delayed-graft function, chronic allograft dysfunction, and tolerance induction. Moreover, several clinical trials were defined to approve the safety and feasibility of the application of MSCs in KT patients as induction therapy and reduce the dosage and duration of immunosuppression therapy to improve long-term graft survival.

KEYWORDS: Kidney transplantation; Mesenchymal stem cells; Immunosuppressive drugs; Acute rejection; Delayed graft function

No. 2023-22: Making Human Pancreatic Islet Organoids: Progresses on the Cell Origins, Biomaterials and Three-Dimensional Technologies

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ABSTRACT

One of the health issues that presents the most societal challenges is diabetes. It is estimated that there are 425 million diabetic patients worldwide, and by 2030, the global incidence rate would rise to 552 million, as forecasted 3. Human recombinant insulin is currently the standard treatment for diabetic patients. Insulin pump devices or numerous daily injections of this basal-bolus therapy which includes a fast-acting insulin given before to meals and a long-acting insulin that supplies basal insulin are used to administer the insulin. Despite attempts to construct a computer-controlled, scheduled closed-loop system that combines continuous glucose monitors and insulin pumps, the system is unable to replicate physiological euglycemia. Because there is a serious lack of transplantable donors, there is still no effective way to cure diabetes, despite the promising results of islet transplantation for insulin-dependent diabetes. Organoid technology has gained a lot of attention recently since it can most closely resemble a human organ in vivo to in vitro state, bridging the gap between biological models at the cellular and tissue/organ levels. Simultaneously, it is anticipated that human pancreatic islet organoids will provide a significant supply of islet transplants. Three essential components are needed to create human islet-like organoids: seeding cells, biomaterials, and three-dimensional structure. In this article, we provide an overview of the latest developments on the origins of cells, biomaterials, and cutting-edge technology used to create human islet organoids. We also go through the benefits, drawbacks, and potential obstacles of these technologies.

KEYWORDS: Pancreatic islet; Organoids; Biomaterials; Three-Dimensional Technologies

No. 2023-23: Renoprotective Effect of Mesenchymal Stem Cells Transplantation in Acute Kidney Injury Induced by Renal Ischemia-Reperfusion

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ABSTRACT

Background: Acute kidney injury(AKI) is characterized by a sudden renal dysfunction that is related to severe tubular and vascular damages. Renal injury induced by ischemia/reperfusion is a common problem in the renal transplantation. Mesenchymal stem cells(MSCs) transplantation is promising new treatment that improve renal damage and mediate repair after acute kidney injury. The aim of this study, assessment of stem cell therapy in acute kidney injury in animal model.

Methods: MSCs were extracted from the bone marrow of male Sprague–Dawley rats, cultured in DMEM, and detected by suitable markers before transplantation. Renal injury induced by 60 minutes' bilateral ischemia followed by 24 hours of reperfusion. Rats randomly divided into three groups (sham, BIR and BIR+BMSCs). BMSCs were immediately injected (1×106 cells, i.p) the end time of ischemia in the BIR+BMSCs group. 24h After of reperfusion, all rats reanestesizied, kidney tissue removed, plasma samples were taken and stored for structural and functional assessment respectively. In addition, histopathological assay was done by H&E staining method.

Results: Structural damages of kidney were characterized as enlargement of urinary space, acute tubular necrosis, vascular congestion, and tubular cell injury after BIR. Plasma levels of blood urea nitrogen (BUN) and creatinine (Cr), as renal functional marker, significantly increased after renal ischemia in the BIR group. Administration of stem cell slightly decreased cellular and vascular damages as well as declined plasma levels of BUN and Cr in the BIR+BMSCs.

Conclusion: The data indicated a highly significant renoprotective effect by mesenchymal stem cells that indicates their therapeutic potential in renal ischemic-reperfusion injures. Therefore, stem cell transplantation improved morphology changes, and attenuated renal functional disturbance in acute kidney injury.

KEYWORDS: Acute kidney injury; Stem cell transplantation; Ischemia-reperfusion injury

No. 2023-24: Kidney The Effect of Self-Management Education through a Mobile Application on Patient's Self-efficacy and Adherence to Medication after Liver Transplantation

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ABSTRACT

Background: One of the causes of liver transplantation failure is a lack of adherence to medication. Recipients can prevent complications during the treatment to a considerable extent by self-management. The present study aimed to determine the effect of self-management through a mobile application on patients' self-efficacy and adherence to medication after liver transplantation.

Methods: This study was an educational trial with intervention and control groups and a pre-test/post-test design conducted on 62 liver transplantation patients with the inclusion criteria in Shiraz from 2020 to 2021. The data collection tools included a demographic characteristics questionnaire, the Chronic Disease Self-efficacy scale (CDSES), and the Basel Assessment of Adherence to Immunosuppressive Medication Scale (BAASIS). First, the CDSES and BAASIS questionnaires were given to the participants of both groups as the pre-test. Afterward, educational information about management and adherence to medication was provided to the intervention group in the form of a mobile application. The control group received the usual nursing care and education. Three months after the pre-test, the questionnaires mentioned above were completed by the participants for the second time. The data were analyzed using SPSS 25.

Results: The mean scores of self-efficacy and its dimensions before and after the intervention were significantly different in both the control and intervention groups (P-value<0.05). Moreover, the mean total scores of self-efficacy and its dimensions after the intervention were significantly different between the two groups (P-value<0.0001). The mean scores of adherence to medications, before and after the intervention, were significantly different between the groups (P-value<0.05). However, after the intervention, no significant difference was observed between the two groups in terms of adherence to medication (P-value>0.05).

Conclusion: Teaching self-efficacy through a mobile application and standard education can affect patients' self-efficacy and adherence to medication after liver transplantation. Therefore, it is recommended that self-efficacy be taught using a mobile application or through traditional methods for patients who are not able to use mobile applications to improve their self-efficacy and adherence to medications and provide services to them.

KEYWORDS: Mobile education; Self-management; Self-efficacy; Adherence to medication; Liver transplantation

No. 2023-25: Therapeutic Drug Monitoring of Mycophenolate in Combination with Cyclosporine or Tacrolimus in Kidney Transplant Patients

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ABSTRACT

Background: Kidney transplantation is usually the preferred treatment option for patients with end-stage renal disease. The narrow therapeutic index drug, mycophenolate, is widely used in immunosuppressive protocols for the prophylaxis of organ rejection in solid organ transplant patients; however, the potential benefits of mycophenolate therapeutic drug monitoring (TDM) in various clinical situations of patients with kidney transplant is still lacking. Calcineurin inhibitors (TCIs) have been shown to affect the level of mycophenolate. Objective: In the present study, we aimed to evaluate the importance of mycophenolate TDM in kidney transplant patients receiving the guideline-recommended doses of mycophenolate in addition to cyclosporine or tacrolimus.

Methods: One hundred kidney transplant patients who were on their first post-transplant month entered into the study. All of the patients received mycophenolate mofetil (Cellcept®) 1 g or mycophenolate sodium (Myfortic®) 720 mg twice daily in combination with cyclosporine or tacrolimus. Blood samples were collected at two time points including days 3 and 14 after transplantation. They were taken before the morning dose of mycophenolate, cyclosporine, and tacrolimus. After centrifugation, the serum fractions were frozen until the assay. At the end of the study, the serum concentration of mycophenolate was measured in all collected samples by a developed analytical method based on spectrofluorimetry.

Results: There was no significant clinical and demographic difference between the two groups of patients receiving cyclosporine or tacrolimus in their regimen. The obtained mean plasma concentration of mycophenolate at days 3 and 14 after transplantation was 2.54±2.36 mg/L and 3.47±3.45 mg/L, respectively; which was in the acceptable therapeutic concentration range.

Conclusion: Monitoring of the trough level of mycophenolate in patients receiving cyclosporine or tacrolimus in their post-transplant regimen showed that the concentration of mycophenolate was in the acceptable therapeutic concentration range (1-3.5 mg/L) in which, no hematologic and gastrointestinal adverse effects were observed. The clinical meaning of the study is that mycophenolate TDM is not necessary in kidney transplant patients receiving the guideline-recommended doses of MMF in addition to cyclosporine or tacrolimus.

KEYWORDS: Therapeutic Drug Monitoring; Mycophenolate; Cyclosporine; Tacrolimus; Kidney Transplant

No. 2023-26: Critical COVID 19 in Liver Transplantation

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ABSTRACT

Background: Considering the importance of assessing solid organ transplant, infected individuals with coronavirus disease 2019 (COVID-19), and the lack of information in this regard, this descriptive study aimed to investigate the clinical features, immunosuppressive agents, and outcomes of liver transplant patients in the critical phase of infection with COVID-19.

Methods: This descriptive cross-sectional study was conducted on 12 critically ill liver transplant recipients referred to Imam Reza and Montaseriyeh hospitals affiliated to Mashhad University of Medical silences, Mashhad, Iran, within 2020-2021. The required data, including demographic and clinical information, were gathered and recorded in a checklist, and the correlations between variables were assessed in SPSS software (version 24).

Results: Hypertension, diabetes, and chronic kidney disease were reported in 83.3% (n=10), 58.3% (n=7), and 41.6% (n=5) of patients, respectively. The administration of Mycophenolic acid was correlated with conjunctivitis (r=-0.67; P=0.02), weakness (r=0.77; P=0.006), and sore throat (r=-0.67; P=0.02). Ground glass opacity was reported in all patients, which was along with consolidation in 90.9% of the cases, and acute pulmonary embolism was found in 36.3% of the subjects. Finally, 66.7% (n=8) of patients passes away. Among immunosuppressive agents, only the use of Mycophenolic acid was correlated with outcome (r=-0.77; P=0.006).

Conclusion: Due to the high rate of mortality among liver transplant recipients in the critical phase of COVID-19, earlier and more aggressive treatment with antiviral and antibacterial agents should be performed in this group of patients.

KEYWORDS: COVID-19; Immunosuppressive; Liver transplantation; Mortality

No. 2023-27: Efficacy of Sinopharm Vaccine among Stem Cell Transplant Recipient

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ABSTRACT

Background: Considering the dearth of research on the complications of Sinopharm coronavirus disease 2019 (COVID-19) vaccine in the immunocompromised individuals and the lack of available data on COVID-19 vaccination from Iran. This study aimed to investigate the complications and efficacy of Sinopharm COVID-19 vaccine in bone marrow transplant (BMT) recipients.

Methods: This was a retrospective cross-sectional study was conducted on 250 patients with BMT who were referred to Montaserieh Hospital, Mashhad, Iran. Among them 53 case who received at least two doses of Sinopharm COVID-19 vaccine from March to January 2021 were entered in this study. The data were extracted from a student dissertation (Code:4000370).

Results: Sinopharm vaccine side effects were reported only in 7.7% of the patients, and Shingles was the only serious side effect of the Sinopharm vaccine, which was observed only in one case.The results also revealed that Sinopharm COVID-19 vaccine side effects were not related to age or gender. Infection with Delta variant of COVID-19 was reported in 7.5% (n=4) and no mortality was reported among them. Vaccine failure was reported in 39.6% of the cases; however, no mortality was reported among patients infected with the Omicron variant of COVID-19.

Conclusion: In summary, it seems that Sinopharm COVID-19 vaccine adverse effects were not serious among stem cell transplant recipients. However, it may lead to some severe complications in the population. Vaccine failure against the Delta and Omicron variants of COVID-19 has been reported among more than one-third of BMT patients; however, no mortality was observed among BMT patients infected with the new variants of COVID-19.

KEYWORDS: COVID-19; Side effects; Transplant; Vaccination; Sinopharm; Stem Cell

No. 2023-28: Manifestations of Aspergillosis in Post-liver Transplant Patients

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ABSTRACT

Background: Aspergillosis is a severe and fatal complication that causes infection in transplant recipients and patients with immunodeficiency syndrome, neutropenia, chronic granulomatosis, and hematologic malignancies. Invasive Aspergillosis has been reported as one of the fungal infections with high mortality in transplant recipients. This study aimed to evaluate the manifestations of Aspergillosis fungal infections in liver transplant patients.

Methods: This Descriptive cross-sectional study was conducted on Ten case of 86 patients with liver transplantation who were infected with Aspergillosis fungal infections. Data were gathered from the medical records of the archive of Montasryieh Hospital, Mashhad, Iran, between August 2019 and August 2020.

Results: In general, 11.6% (n=10) of the patients who had liver transplantation from August 2019 to August 2020 had been infected with Aspergillosis. Only 6.7% of the patients were categorized under the late-onset (>90 days after liver transplantation), and 93.3% of them were early-onset (<90 days after liver transplantation). Aspergillosis fungal infections were suspected on the basis of clinical or radiological signs (possible in 30% of cases; n=3). The probable diagnosis was reported in 60% (n=6), and the proven diagnosis was observed only in one patient. Moreover, 80% of the patients were diagnosed with Pulmonary Aspergillosis, and two patients had pulmonary Aspergillosis in combination with the central nervous system and cutaneous Aspergillosis. A correlation was reported between a comorbid disease and type of Aspergillosis (r=0.69; P=0.02). Voriconazole was effective to treat invasive Aspergillosis in all patients.

Conclusion: The prevalence rate of Aspergillosis is relatively high among liver transplant recipient populations (11%). All recipients infected with Aspergillosis had at least one risk factor, including an underlying disease. It seems that therapy is effective using Voriconazole among transplant patients with pulmonary Aspergillosis.

KEYWORDS: Aspergillosis; Fungal infections; Transplant patients; Voriconazole

No. 2023-29: Post-solid Organ Transplants Central Nervous System Infections

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ABSTRACT

Background: Due to the suppression of immune system in liver and kidney recipiens, these patients are susceptible to various infections, including infections of the central nervous system (CNS). Lack of timely diagnosis of this type of infection increases mortality rate in these patients. The purpose of this study is to investigate clinical, laboratory and radiological manifestations of CNS infections after solid organ transplant in patients admitted to Montaserieh, Imam Reza and Ghaem hospitals, Mashhad, Iran.

Methods: In this cross-sectional study, information of patients who received liver or kidney transplants during the years 1397-1400 was extracted from the archives of Montaserieh, Imam Reza and Ghaem hospitals. Demographic data, transplant and infection prophylaxis drugs, time of infection, symptoms, as well as laboratory and imaging data were evaluated.

Results: A total of 11 cases were found, of which 7 (63%) were male and 4 (37%) were female. There were 4 (36.4%) male patients who received a kidney transplant, 3 (27.3%) male patients who received a liver transplant, and 4 (36.4%) female patients who received a kidney transplant. Of these, 2 transplants (18.2%) were rejected in men and 2 transplants (18.2%) were rejected in women. one case in men and 2 cases in women were re-transplanted. There were 2 cases (18.2%) of early CNS infection and 9 cases (81.5%) of late CNS infection. The types of organisms causing CNS infection were as follows: herpes simplex virus (HSV) (18.18%), aspergillus (9.09%), mycobacterium tuberculosis (TB) (9.09%), cytomegalovirus (CMV) (9.09%), nocardia (9.09%), toxoplasma (9.09%), Ebstein-Barr virus (EBV) (9.09%). In 27.27% of cases, the cause of the infection was unspecified. Fever and headache were the most prevalent clinical manifestations. Three patients had concurrent lung inection. Groups with toxoplasma, CMV, HSV, and unspecified infections, were using prednisolone and patients with EBV, TB, aspergillus, HSV and unspecified infections were using tacrolimus. Azathioprine was being used only in one patient with nocardia infection. All patients had the history of using mycophenolate mofetil drug has. Subjects with CMV, nocardia, toxoplasma and unspecified infections were taking cyclosporine. Only the patient with the CMV infection had a history of using sirolimus. Mortality rate was 36%.

Conclusion: Clinical manifestations of infectious CNS disease, even with life-threatening infections, may be vague and difficult to diagnose. Viral, bacterial, or fungal CNS infections should be promptly identified and treated. Special attention should be paid to brain examination in patients with long-standing pulmonary contamination, unresponsive fever, severe corticosteroid therapy, and frequent transplant rejection. Evaluation of transplant recipients with systemic and CNS infection requires a good understanding of the complexities of modern immunosuppressive therapy. Because immunosuppressive drugs alter the clinical manifestations of infections, it is important to maintain vigilance and pay attention to minor neurologic signs.

KEYWORDS: Infection; Central nervous system; Opportunistic organisms; Solid organ transplantation

No. 2023-30: Registry of Opportunistic Organisms in Transplantation Recipients

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ABSTRACT

The registry is an ongoing and systematic list that includes all individuals from a specific population affected by a specific disease. The registry can be used as a care tool, as it can be used to monitor the course of the disease and provide sufficient data for healthcare managers to plan healthcare. Opportunistic infections in transplant recipients have always been a persistent problem, resulting from long-term immunosuppressive therapies used to suppress the immune response against graft antigens in these individuals. The most common opportunistic organisms in immunosuppressed patients include cytomegalovirus infections, herpes simplex, mycobacteria, Toxoplasma parasites, and Pneumocystis carinii, as well as opportunistic fungi such as Candida albicans and other yeasts, Aspergillus, and Mucorales. Timely and rapid diagnosis of these infections and appropriate treatment initiation are crucial, as delays in either can lead to increased mortality and serious and permanent complications for the patient.

The main objectives of this registry include:

- Creating a demographic, clinical, and laboratory data database on various opportunistic infections in transplant recipients in teaching hospitals affiliated with Mashhad University of Medical Sciences.

- Establishing databases of treatment methods, treatment outcomes, pre-announcement, and treatment-related complications for various opportunistic infections in transplant recipients in teaching hospitals affiliated with Mashhad University of Medical Sciences.

- Creating an infrastructure and database (registry) for research on various opportunistic infections in transplant recipients.

- Networking and enhancing collaboration among specialists in fields related to transplant recipients.

- Facilitating the implementation of randomized clinical trials, descriptive studies, and retrospective studies.

Today, healthcare systems require accurate and comprehensive information for effective management in the field of health. It should be possible to achieve the maximum results with the minimum resources, and this goal is attainable through establishing and developing an accessible registry.

KEYWORDS: Registry; Opportunistic infections; Transplant recipients, Database

No. 2023-31: Assessment and Management of Central Nervous System Fungal Infections in Recipients of Liver Transplantation

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ABSTRACT

Background: Liver transplant recipients, due to being immune-compromised and having chronic co-morbid conditions, are highly susceptible to infections, including those that affect the central nervous system (CNS).

Results: Despite the advancements in diagnostic and treatment methods, patients undergoing liver transplantation still face the risk of post-transplant fungal infections. One of the most challenging aspects of caring for these patients is diagnosing and treating CNS fungal infections. Early detection and treatment of these infections are crucial as they are often diagnosed late and can result in significant morbidity and mortality in this patient group.

Conclusion: This review discusses CNS fungal infections in liver transplant recipients, including opportunistic pathogens, risk factors, manifestations, and prophylaxis.

KEYWORDS: Transplant recipient; Liver transplantation; Risk factors; Central nervous system

No. 2023-32: Sinopharm Vaccine among Liver and Kidney Transplantation

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ABSTRACT

Background: There are various vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, vaccination may lead to some complications. This study aimed to investigate the complications of transplant recipients who received Sinopharm COVID-19 vaccine.

Methods: This was a retrospective cross-sectional study conducted among 667 transplant recipients (211 liver transplant recipients and 456 kidney transplant recipients), who received the Sinopharm COVID-19 vaccine during March to August 2021 and had medical records in Montaserieh Hospital, affiliated to Mashhad University of Medical Sciences, Mashhad, Iran. The demographic and clinical information as well as patient's symptoms after each dose of the vaccine were recorded.

Results: Only 16.8% and 13.7% of the patients experienced some symptoms following the first and second doses of Sinopharm vaccine, respectively. No significant difference was observed between patients younger than 50 years and those aged 50 years and over in terms of complication rate of Sinopharm vaccine (P>0.005). Vaccine failure was reported in 10% of the cases; however, mortality rate due to infection with the Delta variant of COVID-19 in this population was reported to be 0.7%.

Conclusion: Based on the obtained results, adverse reactions of the Sinopharm COVID-19 vaccine are generally mild, predictable, and non-life-threatening both in the first and second doses. Vaccine failure was reported in 10% of the cases; however, mortality due to infection with the Delta variant of COVID-19 was reported in less than 1% of the cases.

KEYWORDS: COVID-19; Side effects; Transplant; Vaccination

No. 2023-33: Chronic Kidney Disease Post-Liver Transplantation: The Associated Risk Factors

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ABSTRACT

Background: Liver transplantation is a well-established life-saving procedure for end stage liver insufficiency patients. According to OPTN/SRTR annual data report in 2020, concurrent with covid-19 pandemic, though transplant program activity, waitlist and related outcomes were affected, still 8906 liver transplants were performed in United States. Over the past decade, short and long-term outcomes after liver transplant continued to improve. However, chronic kidney disease (CKD) and end stage renal disease as long-term complications still happen frequently in this population.

Methods: In order to evaluate the CKD outcomes affecting post-LT in recipients, related published studies were investigated through ISI Web of Science, PubMed/Medline, Google Scholar, and Scopus. Key words of the risk factors of CKD after liver transplantation were considered.

Results: Multiple risk factors play role in post-non-renal transplant CKD. But one of the most repeated risk factors is renal function in recipients prior to liver transplant. As pre-operation renal dysfunction by renal perfusion impairment, disturbance of biological markers and more complicated operation can lead to post-LT renal dysfunction at first year. In addition, presence of diabetic mellitus as a pivotal risk factor leading to CKD after liver transplant is associated with micro and microvascular complications causing long-term damage in different organs with significant reduction in survival rate. Moreover, recipients with Hepatitis C (HCV) infection as the cause of liver transplant had higher chance of progressing to CKD, although the exact mechanism of that is still unclear some studies indicated that HCV related kidney damage caused by disposition of immune complex.

Conclusion: Diabetic mellitus, renal function, and HCV are three major risk factors leading to CKD after liver transplant. Risk assessment of the renal function before liver transplantation can improve by reduction and maintenance of modifiable risk factor.

KEYWORDS: Chronic kidney disease; Diabetic mellitus; Hepatitis C; Liver transplantation; Renal function

No. 2023-34: The Role of Regenerative Medicine in Organ Transplantation

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ABSTRACT

Background: As life expectancy and the prevalence of chronic illnesses increases, organ transplantation is expected to climb as well. The effectiveness of the existing allograft transplantation strategy is being challenged by technologies inspired by regenerative medicine.

Methods: The National Library of Medicine's MEDLINE PubMed interface was used to do a literature review. The findings were analyzed for their applicability to organ bioengineering improvements in order to inform the examination of regenerative medicine advancements that impact organ transplantation. To illustrate the scarcity and necessity of transplantable organs, data reports from the Scientific Registry of Transplant Recipient and Organ Procurement Transplantation Network from 2010 to 2022 of kidney, pancreas, liver, heart, lung, and intestinal transplants performed and patients presently on waiting lists for respective organs were examined.

Results: The goal of regenerative medicine technology is to restore and grow organs that aren't working well. Achieving a condition free of immunosuppression is one objective in order to enhance quality of life, lower problems and toxicities, and do away with the need for lifetime anti-rejection treatment. Three-dimensional printing, interspecies blastocyst complementation, and decellularization to create acellular scaffolds that will serve as a template for organ production are examples of novel approaches. An advancement in stem cell science, induced pluripotent stem cells address the limitations of other progenitor cells that do not possess pluripotency as well as the ethical issues surrounding embryonic stem cells. Technologies in regenerative medicine have potential for a variety of uses and domains, including enhancing the viability of already-existing ex vivo transplanted organs, growing new tissue or organs, modeling disease states, and encouraging the regeneration of native cell lines.

Conclusion: Enhancing knowledge of organogenesis, in vivo regeneration, regenerative immunology, and long-term monitoring of implanted bioengineered organs is essential for the future of organ bioengineering.

KEYWORDS: Organ transplantation; Regenerative medicine; Bioengineering

No. 2023-35: The Importance of MicroRNAs in Acute Myeloid Leukemia and Hematopoietic Stem Cell Transplantation

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ABSTRACT

Acute myeloid leukemia (AML) is a hematological malignancy that develops from an excessive accumulation of abnormal myeloid progenitors in the peripheral blood and bone marrow. Small non-coding RNAs (miRNAs) play an essential role in the post-transcriptional regulation of gene expression. Dysregulated or aberrant miRNA expression has been described in the initiation and progression of a broad spectrum of hematologic malignancies and severe post-transplant complications in patients receiving hematopoietic stem cell transplantations (HSCT). It is shown that miRNAs are playing role in nearly all aspects of AML disease development. An increasing quantity of evidence supports the significance of miRNAs in malignant hematopoiesis via the control of oncogenes and tumor suppressors involved in proliferation, differentiation, and cell death. In this review, we provide recent research on the role of dysregulated miRNA expression in the etiology of AML. We present data on the clinical value of abnormal miRNA expression profiles in hematologic monitoring of AML. Furthermore, we will explore the growing function of miRNAs in HSCT and severe post-HSCT consequences, such as graft-versus-host disease (GvHD). This therapeutic potential of miRNA-based strategy in hemato-oncology will be discussed, including research using specific antagomirs, mimetics, and circular RNAs (circRNAs). These observations have led to the study of miRNAs as novel diagnostic and prognostic biomarkers that may result in better diagnosis and patient outcomes.

KEYWORDS: microRNA, Acute myeloid leukemia;Hematopoietic stem cell transplantation; Graft-versus-host disease; miRNA-based approach

No. 2023-36: Investigating New Methods in Preserving Ovarian Tissue Before Ovarian Transplantation

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ABSTRACT

New methods of ovarian tissue protection have emerged in recent years as a promising technique to preserve fertility women undergoing cancer treatments or other conditions affecting ovarian function. These methods involve the isolation and cryopreservation of ovarian tissue, which can then be reimplanted back into the patient at a later time. One such method involves the use of natural substances known as antioxidants, can help prevent damage to the ovarian tissue caused by chemotherapy or. Other methods include the use of drugs that inhibit apoptosis (programmmed cell death), as well as novel techniques for cryopreservation, such as slow freezing and vitrification. While these methods are still the experimental stage, they hold great potential as a way to preserve fertility in facing cancer treatment or other conditions that may damage ovarian function.

KEYWORDS: Tissue preservation; Ovarian Transplantation; Slow freezing; Vitrification

No. 2023-37: The Angiotensin Type 1 Receptor: A Drug Target to Reduce the Risk of Organ Transplant Rejection

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ABSTRACT

Allograft rejection is one of the main problems that must be overcome. Evidence suggests a role of the local renin-angiotensin system (RAS) in the progress of chronic allograft injury. Angiotensin II, generated by the renin-angiotensin system, is well-known as a major regulator molecule to control the blood pressure and fluid system. Evidence suggests that this bioactive molecule and its receptor increase the risk of tissue injuries and organ transplant rejection through different molecular mechanisms such as activation of innate and cellular immunity, upregulation of inflammatory pathways, and accumulation of extracellular matrix by expression pro-fibrotic molecules like transforming growth factor β (TGF-β) to increase the risk of fibrosis. Based on these findings, AT1R antagonists might have therapeutic potential to prevent the risk of tissue injuries and allograft rejection by regulating immune response, inflammation pathway, and fibrogenesis to improve organ functions.

KEYWORDS: Organ transplant rejection; Angiotensin II; Angiotensin type 1-receptor; Inflammation; Fibrosis

No. 2023-38: Association between C4d and Donor-Specific HLA Antibodies in Renal Transplant Patients

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ABSTRACT

Background: We carried out a retrospective study of C4d staining in paraffin sections from renal transplant biopsies to determine the association between C4d staining, donor-specific antibodies (DSA), histological features, and graft outcome.

Methods: We studied 60 patients who had been biopsied for graft dysfunction. Biopsies were classified using Banff 2019 criteria and features suggestive of antibody-mediated rejection were noted. Paraffin sections were stained with a polyclonal antibody using an immunoperoxidase technique. The presence of DSA in concurrent sera was determined by single antigen assay and clinical data were reviewed.

Results: Of the 45 cases, 9% showed diffuse and 16% showed focal C4d positivity. The grafts failed in 33% of the diffuse ($P<0.025$), 25% of the focal, and 5% of the negative group at between one month and 4 years post transplantation. Only patients in the group with diffuse C4d positivity had concurrent DSA (five cases, $P<0.001$).

Conclusion: We demonstrated a significant association between diffuse C4d staining, production of DSA, and graft failure. Although the concurrent detection of DSA and C4d positivity is uncommon in our patients, these results indicate that outcome in this group is poor and they may benefit from therapies directed at the humoral response.

KEYWORDS: C4d staining; HLA-specific antibodies; Renal transplant

No. 2023-39: Factors Associated with Tumor Lysis Syndrome in Children with Hematologic Malignancies

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ABSTRACT

Background: Tumor lysis syndrome (TLS) is a severe complication of hematologic malignancies. Different factors have been considered as risk factors for progression to TLS. Few studies have evaluated the factors that increase the risk of developing TLS in children with hematologic malignancies.

Methods: In a five-year period, children ≤18 years with hematologic malignancies in the oncology ward of Dr. Sheikh Hospital were assessed for TLS according to the Crigio-Bioshop criteria (2004). The roles of the age, gender, type of tumor, percent of blast cells in peripheral blood smear and bone marrow, serum levels of LDH, and WBC count in the occurrence of TLS were evaluated.

Results: In total, 249 cases were enrolled. Laboratory pre- and post-chemotherapy data were available in 231 and 197 cases, respectively. They included 55.8% boys. The types of tumor included ALL (83.5%), AML (8.4%), Hodgkin and non-Hodgkin lymphoma (each 3.2%), and Burkitt lymphoma (1.2%). The pre-chemotherapy TLS happened in 35 cases (15.15%). Of four cases (11.4%) with clinical TLS, one died and one underwent hemodialysis. The post-chemotherapy TLS happened in 43 cases (21.8%). Three cases (7%) had clinical TLS, two died and one underwent hemodialysis. The median WBC count and serum LDH levels were significantly higher in cases with pre-chemotherapy TLS compared to those without (P=0.0001 and P=0.001, respectively). In addition, the percent of blast cells in the peripheral blood smear was significantly higher in cases with versus those without TLS (P=0.038). Patients with post-chemotherapy TLS were significantly younger than those without (P=0.037). In addition, the median serum levels of LDH were significantly higher in the first versus the second group (P=0.001). Both pre and post-chemotherapy TLS did not correlate with the type of tumors (P=0.475 and P=0.656, respectively).

Conclusion: The median WBC count, serum LDH levels, and percentage of blast cells in peripheral blood smear significantly correlated with the occurrence of pre-chemotherapy TLS. Whereas, younger age, the median serum LDH levels significantly correlated with post-chemotherapy TLS.

KEYWORDS: Tumor lysis syndrome; Hematologic malignancy; Children

No. 2023-40: Revolutionizing Liver Transplantation: Harnessing the Power of 3D Printed Liver Models

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ABSTRACT

The liver possesses two essential functional properties that play a key role in maintaining the homeostasis of the body. Firstly, it serves to centralize the systemic metabolism, thereby exerting control and modulation over the functioning of both the central and peripheral neurological systems, the immunological system, and the endocrine system. Liver diseases are a prominent factor in global mortality rates. Liver transplantation is widely recognized as the accepted therapeutic approach for individuals with end-stage liver failure. However, a limited number of available liver donors and the necessity for long-term immunosuppressive therapy create significant obstacles to the broad use of allogeneic liver transplantation. As a result, there is a growing demand for alternate approaches such as tissue engineering, which are now being actively investigated. The domain of liver tissue bioengineering encompasses numerous techniques that are directed toward advancing therapeutic interventions for liver disorders. The primary goal of liver engineering is to establish suitable hepatic models that can reveal the pathological mechanisms behind liver disorders, such as liver organoid disease models, cancer models, and virus-infected models. Just like in vivo environments, three-dimensional (3D) models facilitate several cellular processes such as cell-cell and cell-matrix interactions, cellular migration, chemotaxis, traction, and integrin adhesions. Additionally, these models are capable of replicating soluble growth factor gradients, which play a crucial role in supporting cellular differentiation and maturation. Furthermore, The ultimate goal of liver tissue engineering is to develop transplantable liver tissue that can effectively replace the damaged area of the liver and reinstate its hepatic functionalities.The utilization of 3D bioprinting technology allows for the creation of biomimetic tissues and implants through the incorporation of biomaterials, growth factors, and living cells. These components can be printed in a specified arrangement to generate the desired tissue structure, or alternatively, can be printed onto an existing 3D matrix, commonly referred to as a scaffold. Laser-based techniques, inkjet printing, and microextrusion printing are the main direct writing techniques employed for the fabrication of cells in the field of bioprinting. The selection of these techniques is primarily due to their ability to readily accommodate the cultivation environment, generate high-resolution cell structures, and, in numerous cases, promote the production of three-dimensional scaffolds for cell growth. Significant progress has been made in liver tissue engineering with the previously mentioned methodologies; yet, further efforts are necessary to address existing challenges. Our goal in this article was to investigate the use of bioprinting to create 3D liver models in the fields of regenerative medicine and tissue engineering, particularly liver transplantation and drug testing.

KEYWORDS: Liver; Transplantation; Bioprinting; 3D liver model

No. 2023-41: Reducing Liver Transplantation Rates for HCC Patients with Targeted Drug Delivery to Liver Cancer Cells

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ABSTRACT

The management of Hepatocellular Carcinoma (HCC), a primary liver cancer, poses a significant challenge in healthcare due to its often advanced stage at diagnosis. Liver transplantation has been a viable treatment option for eligible patients, but donor scarcity and stringent criteria limit its availability. To address this, researchers and clinicians have been exploring innovative approaches to reduce the necessity of liver transplantation for HCC patients.

One promising strategy involves the development of targeted drug delivery systems tailored specifically for liver cancer cells. This approach capitalizes on advancements in nanotechnology and drug delivery techniques to improve the precision and efficacy of cancer treatment. By delivering therapeutic agents directly to the tumor site, targeted drug delivery minimizes collateral damage to healthy liver tissue, potentially preserving liver function and expanding the therapeutic window.

So far, researchers have explored several types of nanocarriers, such as organic and inorganic nanoparticles (magnetic, metallic, etc.), lipids, polymers, and aptamers, to improve drug delivery to liver cancer cells. These carriers can be engineered to carry chemotherapeutic drugs, immunotherapies, or gene therapies, allowing for a multifaceted attack on cancer cells while sparing healthy liver parenchyma. Furthermore, molecular profiling and biomarker discovery advances enable patient-specific treatment strategies, further personalizing therapy.

The idea of delivering drugs directly to the affected area for patients with HCC has potential, but it still requires a lot of research. Ongoing studies are being conducted to evaluate its safety, effectiveness, and long-term effects. The aim is to decrease the need for liver transplantations in HCC patients by providing better and less invasive treatment options. As research advances, the possibility of improving the diagnosis and quality of life for people with HCC is becoming more achievable, providing a brighter future with fewer transplantations and more targeted therapies.

KEYWORDS: Hepatocellular carcinoma; Liver transplantation; Nanocarriers; Targeted drug delivery systems

No. 2023-42: Prognostic Value of Nutrition Indices in Candidate Patients for Liver Transplantation

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ABSTRACT

Background: Orthotopic liver transplantation (OLT) is a life-saving procedure in cases of liver failure and organ allocation is important in these patients. Therefore, scoring systems is needed to enhance devoting organ to these patients. Since anthropometric indices play important roles in predicting prognosis of cirrhotic patients, we introduced a scoring system utilizing anthropometric indices to predict survival in cirrhotic patients.

Methods: The clinical and anthropometric information of 64 patients referred to Ibn Sina Transplantation Center were followed up for three months. The Least Absolute Shrinkage and Selection Operator (LASSO) logistic regression model was used to devise the new scoring system. The new model was compared to Model for End-stage Liver Disease (MELD) regarding survival rate of the cirrhotic patients.

Results: The mean age of patients was 46.50±12.871 years old. Hand Grip (HG), Skeletal Muscle mass Index (SMI), Mean Arterial Pressure (MAP), serum sodium, and total bilirubin were included in the model scoring system that utilizes the area under the curvature of the Receiver Operating Characteristic (ROC) curve and could significantly predict survival in cirrhotic patients when compared with MELD scoring system.

Conclusion: We have introduced a new score in prediction of survival probability in cirrhotic patients that can help optimizing transplant resources and in decision making of liver allocation.

KEYWORDS: Nutrition Indices; Liver Transplantation; Survival; Cirrhotic patients

No. 2023-43: Prevalence of Vesicoureteral Reflux and Renal Scarring in A Pediatric Population With Urinary Tract Infections: Comparing Patients ≤5 Years With Those >5 Years of Age

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ABSTRACT

Background: Urinary tract infections (UTI) is a serious clinical problem in childhood. The highest incidence of UTI is seen in two age groups: under one year and 2-4 years. Early identification of renal scar is very important because scarring and reduced kidney function can cause serious health problems and reduced quality of life. Comparing frequency of vesicoureteral reflux and renal scarring in children ≤5 years affected by urinary tract infection versus those >5 years.

Methods: A longitudinal study was performed on children under 18 years of age with diagnosis of urinary tract infection from October 2003 to October 2016. Cases who underwent kidney-bladder ultrasound and voiding cystourethrogram were identified.Tc-99m DMSA was used in patients with febrile urinary tract infection, those with vesicoureteral reflux, or in the case of renal scarring in kidney ultrasound. patients without VUR and those or non-febrile UTIs, were much less likely to be evaluated with a DMSA scan compared those with high grade VUR and/or febrile UTI, since DMSA scans were only performed in 47% of patients, so we have selection bias . Patients with neurogenic bladder, urinary obstruction, and undetermined age at presentation were excluded.

Results: Totally, 816 patients were enrolled including 719 girls (88.1%) and 97 boys (11.9%), aged 33.26±32.47 months. The age groups ≤5 and > 5 years consisted of 675 (82.7%) and 141 patients (17.3%), respectively. Vesicoureteral reflux was significantly more common in group ≤5 years versus >5 years (P<0.0001). The frequency of high grade vesicoureteral reflux did not differ significantly between the groups (P=0.888). Renal scarring was found in 33.4% of patients and no significant difference existed in the frequency between the groups (P=0.523). Kidney units with severe scarring were significantly more prevalent in patients >5 years than those ≤5 years (P=0.024).

Conclusion: Vesicoureteral reflux was more prevalent in the patients ≤5 years, but high grade vesicoureteral reflux was as common in children >5 years as in those ≤5 years. Furthermore, no risk factor for renal scarring was found, but kidney units with severe scarring were more prevalent in cases >5 years., the overall lower prevalence of VUR in patients with renal scarring in the >5yo group may have be impacted by the possibility that prior VUR in younger years may have resolved spontaneously.

KEYWORDS: Urinary tract infections; Children; Age; Vesicoureteral reflux; Renal scarring

No. 2023-44: The Relationship Between Idiopathic Hypercalciuria and Recurrent Urinary Tract Infection in Children

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ABSTRACT

Background: Urinary tract infection (UTI) is a very common and important issue in children and the second cause of bacterial infection in this group. Studies have been conducted to assess the relationship between hypercalciuria and recurrent UTI; however, controversies have remained. The aim of our study is to assess the relationship between idiopathic hypercalciuria and recurrent UTI in 6 months to 16 years old children, who referred to Dr. Sheikh and Akbar hospitals.

Methods: This case-control study was conducted between January 2018 to December 2020. Fifteen children with recurrent UTI (2 or more infections during 6 months or 3 or more infections during one year) as the case control were compared with 50 healthy children without the history of UTI. After a negative urine culture, the random calcium/creatinine ratio was measured and ratios more than 0.8, 0.6, 0.5, and 0.2 were considered as hypercalciuria in ≤ 6-months children, 7 to 12-months children, 12 to 24-months children, and ≥ 24-months children, respectively. In order to rule out secondary hypercalciuria, the serum levels of calcium, phosphorus, alkaline phosphatase, urea, and creatinine were assessed. The two study groups were compared in case of hypercalciuria. Logistic regression was used to assess the relationship of hypercalciuria with recurrent UTI. p values less than 0.05 were considered significant.

Results: Totally, 50 cases and 50 controls were enrolled in the study. There was no significant difference in case of age (p=0.233), gender (p=0.835), and calcium to creatinine ratio (p=0.245) between the two study groups. The isolated germs in urinary culture were E.coli with 37 cases (74.0%), Klebsiella with 8 cases (16.0%), Proteus with 2 cases (4.0%), pseudomonas with 2 cases (4.0%), and entrobacter with 1 case (2.0%). In case of the distribution of abnormal and normal calcium/creatinine ratio, there was a significant difference between cases and controls (p=0.046). However, there was no significant relationship between calcium/creatinine ratio and urinary tract infection (OR=0.219; 95% CI= (1.088-0.044); p value=0.063).

Conclusion: In conclusion, there was no significant relationship between hypercalciuria and recurrent UTI in pediatric cases, in our study. However, further studies are needed to confirm these results.

KEYWORDS: Hypercalciuria, Recurrent urinary tract infection, Children, Calcium/creatinine ratio

No. 2023-45: Comparison of Enhanced and Manual Urinalysis for Detecting Urinary Tract Infections in Children

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ABSTRACT

Background: Urinary tract infections (UTIs) are among the most common bacterial infections in children. Urinalysis (UA) is a beneficial test for the preliminary diagnosis of UTIs. The presence of bacteriuria in UA can be determined by either an enhanced (using uncentrifuged Gram-stained specimens) or manual (using centrifuged specimens) technique. However, the diagnostic performance of enhanced UA is not well-established in childhood UTIs. To assess the ability of enhanced and automated urinalysis to detect UTIs in children.

Methods: This cross-sectional study was conducted on 191 children with the symptoms of UTI referred to Dr. Sheikh Hospital, Mashhad, Iran, from 2018 to 2019. Standard urinalysis, enhanced urinalysis, and quantitative urine culture were performed on specimens. A positive enhanced UA test was defined as ≥ 10 white blood cells per mL of urine and the presence of any bacteria per 10 high-power microscopic fields of a Gram-stained smear. A positive manual UA test was defined as ≥ 5 white blood cells per high-power field. The results of standard and enhanced UA were compared with urine culture findings to determine the accuracy of these two methods in detecting UTIs. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were determined for each test.

Results: The results showed that the prevalence of UTI was 23%. Enhanced UA retrieved a sensitivity of 97.7%, specificity of 93.1%, PPV of 81.1%, and NPV of 99.3% for detecting UTIs. In standard UA, sensitivity, specificity, PPV, and NPV were 90.9%, 80.7%, 57.1%, and 96.6% for pyuria, 56.8%, 98.6%, 92.5%, and 88.4% for the nitrite test, 72.7%, 94.5%, 80%, and 92% for the leukocyte esterase test, respectively.

Conclusion: Enhanced UA had higher sensitivity, specificity, PPV, and NPV than standard UA.

KEYWORDS: Enhanced method; Manual method; Urinary tract infections; Children

No. 2023-46: Investigating the Outcomes of Transplantation using Hematopoietic Stem Cells obtained from Peripheral Blood and Bone Marrow Sources

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ABSTRACT

Background: Hematopoietic stem cell transplantation (HSCT) is an available therapeutic approach for hematological disorders and malignancies. Bone marrow (BM) and peripheral blood (PB) are the principal sources for supplying the stem cells needed for transplantation, and the latter has attracted the attention of clinicians due to some advantages, especially ease of collection. Nevertheless, the equivalence, efficiency, and satisfaction of the results of stem cell transplantation obtained from PB versus those obtained from BM are debatable. The purpose of this study was to compare the advantages and disadvantages listed in previous studies for each of these two mentioned approaches, which may help health professionals make an informed decision and choose a targeted procedure for HSCT candidates.

Methods: The necessary data for this review were obtained by searching the articles published between 2010 and 2023 in databases including Pubmed, Web of Science, Scopus, and Google Scholar.

Results: The results of related studies indicated that receiving hematopoietic stem cells obtained from PB has generally brought benefits to transplant recipients, including reducing the risk of transplant failure, faster hematological recovery, more appropriate neutrophil and platelet recovery, and a lower relapse rate. This approach especially has anti-leukemic effects and significant improvement in high-risk blood malignancy patients. Nevertheless, stem cells collected from the BM have been preferred over stem cells obtained from PB in terms of reducing the risk of developing chronic graft-versus-host disease (cGVHD) and also the incidence of treatment-related side effects in transplant recipients. Also, all studies have confirmed the lack of difference in overall survival, event-free survival, and recurrence-free mortality in transplanted patients using cells from both sources.

Conclusion: The findings of this study suggest that the use of PB as a source of hematopoietic stem cell extraction has potential benefits for both donors and recipients. However, solving its remaining challenges, especially the risk of cGVHD, requires more research and experiments so that this method completely replaces stem cell transplantation from BM. Until then, transplant planning should be done according to the patient's condition and the potential advantages and disadvantages of both mentioned approaches.

KEYWORDS: Transplantation; Bone Marrow; Peripheral blood; Stem cell

No. 2023-47: Factors Comparison of Health Anxiety Levels and Quality of Life of Living Donors before and after Liver Transplant Surgery: A Cross Sectional Study

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ABSTRACT

Background: Partial liver transplantation is one of the standard methods for liver transplantation. This surgical procedure is performed from a living person to a sick person, which can lead to physical and mental challenges affecting the quality of life of donors. To compare the level of health anxiety and quality of life of liver donors before and after liver transplant surgery.

Methods: This descriptive cross-sectional study was performed on 45 liver donors referred to Shiraz Organ Transplant Hospital between 2019 and 2020. Standard questionnaires of demographic information, health anxiety and quality of life were used to collect data by convenience sampling. Descriptive and inferential statistics tests were used to analyses the data. A significance level was considered $P<0.05$.

Results: Patients' quality of life score (in comparison with the overall score and with the subgroups) decreased significantly ($p=0.001$) after liver donation. Also, patients' health anxiety scores (in comparison with the overall score and with the subgroups) increased significantly after surgery ($p=0.001$).

Conclusion: The implementation of awareness programs before and after surgery and purposeful and long-term follow-up, as well as the use of empowerment programs to increase the level of health and quality of life of these people can be a comprehensive and appropriate approach for hospital officials in order to improve health and quality of life after organ donation.

KEYWORDS: Life quality; Living donors; Liver transplantation

No. 2023-48: Liver Transplant Recipients Exhibit Notably Distinct Vancomycin Pharmacokinetics

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ABSTRACT

Background: Vancomycin is the preferred antibiotic for combating numerous gram-positive bacterial infections; however, its administration poses a heightened risk of acute kidney injury (AKI) among patients. Furthermore, the pharmacokinetic profile of vancomycin varies substantially between liver transplant recipients (LTRs) and the general populace. Hence, precise therapeutic drug monitoring (TDM) of vancomycin is imperative within this patient cohort. The primary aim of this study was to evaluate vancomycin pharmacokinetics in LTRs and its association with AKI risk.

Methods: In this prospective study encompassing 34 LTRs, blood samples were systematically collected from patients administered vancomycin at 12-hour intervals, coupled with a loading dose ranging from 20-35 mg/kg and a maintenance dose ranging from 15-20 mg/kg. These samples underwent analysis through high-performance liquid chromatography (HPLC). Subsequently, critical pharmacokinetic parameters, including the area under the concentration-time curve (AUC), were computed. The study also probed into the occurrence of AKI and its pertinent risk factors.

Results: The mean observed values for vancomycin volume of distribution (Vd), clearance (Clv), half-life (t 1/2), and elimination constant (k 1/2) were 1.08 ± 0.66 L/kg, 4.91 ± 2.98 L/h, 12.15 ± 6.63 h, and 0.08 ± 0.045 h-1, respectively. All these pharmacokinetic parameters exhibited significant disparities in LTRs compared to the general population. The incidence of AKI was 44.1%, surpassing that observed in healthy individuals. Factors influencing AKI occurrence encompassed trough and intermediate concentrations, urinary tract infection (UTI), k1/2, t1/2, AUC, length of hospital stay, serum albumin level, baseline total and direct bilirubin concentrations.

Conclusion: The distinctions in pharmacokinetic parameters between LTRs and the general population underscore the imperative nature of vancomycin TDM for all patients.

KEYWORDS: Liver transplant; Vancomycin; Pharmacokinetics

No. 2023-49: Advancements in the Role of Natural Killer Cells in Allograft Tolerance in Solid Organ Transplantation

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ABSTRACT

Acute cellular rejection can be prevented by immunosuppressive regimens, but they have not been successful in controlling anti-donor antibody expansion and chronic organ rejection. Previous attempts to enhance allograft tolerance have focused on various suppressive mechanisms, including T cell depletion, regulatory T cell increase, and hematopoietic stem cell transplantation to promote tolerance and create donor chimerism. However, none of these approaches have resulted in durable and safe acceptance of donor organs.

Recent developments and accumulating evidence suggest that natural killer (NK) cells may play a crucial role in inducing and maintaining tolerance. Although NK cells are involved in the host's immune response to infections such as cytomegalovirus in transplant recipients, they have the potential to be a promising approach for NK cell therapy in clinical transplantation.

NK cells can proliferate and target allogeneic cells through the production of specific cytokines and antibody-dependent cellular cytotoxicity (ADCC) upon solid organ transplantation. Depending on the subsets of NK cells expanded and their ability to lyse allogeneic cells, secrete chemokines and cytokines, they can either induce the expansion of pro-inflammatory Th1 cells or regulatory Th2/Treg cells, thus influencing the balance of alloimmunity towards rejection or tolerance.

NK cells also contribute to tolerance by suppressing professional antigen-presenting cells, inducing regulatory T cells, and upregulating IL-10. In kidney allografts, NK cells inhibit proinflammatory immune responses, and their depletion can lead to tolerance failure in islet allografts. Additionally, NK cells can initiate tolerance by reducing $CD8^+$ effector memory T cells through competition for IL-15 cytokine usage.

Given that current clinical immunosuppressive agents have little impact on NK cell function, adoptive transfer studies involving NK cells have gained considerable attention in hematopoietic stem cell and solid organ transplantation. NK cells have demonstrated antiviral effects against cytomegalovirus and tumor relapse without causing graft-versus-host disease, and maybe NK cells could have a role in Induction tolerance post organ transplant. Moreover, NK cells could be produced as a living drug for cell therapy, making them a potential candidate for future therapies targeting NK cells in human transplantation.

KEYWORDS: Natural killer cells; Allograft tolerance; Solid organ transplantation

No. 2023-50: Sensitivity and Specificity of Onen Grading System for Hydronephrosis in Predicting Vesicoureteral Reflux (VUR) and High-grade VUR

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ABSTRACT

Background: An incidence of 38% for vesicoureteral reflux (VUR) in prenatal hydronephrosis has been reported. We aimed to determine the sensitivity and specificity of hydronephrosis gradings in predicting VUR and high-grade VUR. Also, defined the incidence of VUR and high-grade VUR in children presented with hydronephrosis.

Methods: A cross-sectional study was designed in children <18 years with hydronephrosis from January 2009 to 2019 in the nephrology clinic of a tertiary hospital. Children underwent VCUG enrolled. Cases with nephrolithiasis, and prenatal hydronephrosis were excluded. Grading of hydronephrosis was done according to the Onen grading system of hydronephrosis (2007).

Results: 313 cases were enrolled in the study. Girls accounted for 52.4%. The median age of patients was 4 years. Hydronephrosis was reported in 67.1% of kidney ureter units (KUUs). It was grades one to four in 39.75%, 50.7%, 7.15%, and 2.4% of KUUs, respectively. The frequencies of VUR and high-grade VUR were 38.6%, and 9.9%, respectively. Gender did not correlate with the VUR and high-grade VUR (P> 0.05 for both). The VUR and high-grade VUR were significantly more prevalent in patients presenting with urinary tract infections versus abdominal pain or lower urinary tract symptoms (P<0.001 and P= 0.047, respectively). The median age in VUR cases was significantly lower than those without (P= 0.016). The VUR and high-grade VUR were significantly more common in KUUs with compared to those without hydroureteronephrosis (P<0.0001 for both). The sensitivity of hydronephrosis grades for VUR was low (1.75-31.75%). The specificity was 65.2-98.5%. For high-grade VUR, they were 5.1-38.45%, and 65.3-98.6%, respectively.

Conclusion: Age, hydro ureter, and clinical presentation significantly correlated with VUR and high-grade VUR in patients with hydronephrosis. The sensitivity of hydronephrosis grades for predicting VUR and high-grade VUR were low, although their specificities were good.

KEYWORDS: Children; Hydronephrosis; Onen grading system for hydronephrosis; Vesicoureteral reflux

No. 2023-51: The Impact of the Multi-drug Resistance-1 Gene Polymorphism on the Pharmacokinetics of Tacrolimus on Kidney Recipients

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ABSTRACT

Background: The management of calcineurin inhibitors (CNIs) is a challenging issue in organ transplantation. The under-dosing of CNIs may lead to acute rejection while their over-dosing increases the risk of nephrotoxicity due to inter-individual differences in response to the drug. This study aimed to evaluate the impact of the multi-drug resistance-1 (MDR-1) gene polymorphism on the pharmacokinetics of tacrolimus and the ratio of concentration per dose of tacrolimus (C/D ratio) in a group of kidney recipients in the North-west of Iran.

Methods: Sixty-five renal transplantation recipients were included. The polymerase chain reaction method was used to amplify the loci of interest.

Results: The frequency of the C and T alleles in the MDR-1 C3435T gene was 79.23 and 20.77%, respectively. Three of the carriers were fast metabolizers with a 0.91±0.11 C/D ratio and two patients were slow metabolizers with a 1.7±0.16 C/D ratio.

Conclusion: Overall, no significant correlation was found between MDR-1 C3435T polymorphism and C/D ratios of tacrolimus, viral infections, and graft rejection.

KEYWORDS: Renal transplantation; Calcineurin inhibitors; Tacrolimus; Multi-drug resistance-1

No. 2023-52: Aquaporin 5 (−1364A/C) Promoter Polymorphism in Renal Transplant Recipients with CMV Infections

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ABSTRACT

Background: Cytomegalovirus (CMV) infection occurs chronically in kidney transplant recipients. Aquaporin 5 (AQP5) gene polymorphism impacts immune cell migration and the mechanisms of inflammation. Therefore, it is involved in the pathogenesis of CMV infection in kidney transplant recipients. This study aimed to evaluate the effect of AQP5 (-1364A/C) polymorphism in kidney recipients.

Methods: In this study, 150 kidney recipients were included (50 transplant recipients with the viral infection and 100 recipients without viral infection), and 50 healthy individuals. Blood samples were taken from participants and the AQP5 (-1364A/C) polymorphism was examined by amplification-refractory mutation system (ARMS)-PCR.

Results: Diabetes mellitus was the most common cause of renal failure in the studied patients. The mean CMV virus titer in patients was 356 28 285. There was no significant association between the presence of the CMV virus and APQ5 genotype (P=0.350) and C and A alleles (P=0.364).

Conclusion: The results of our study showed that the AC and CC genotypes as well as the C allele had no significant relationship with the occurrence or presence of CMV virus in transplant patients.

KEYWORDS: Kidney transplantation; Aquaporin 5; Cytomegalovirus