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Meeting Abstracts

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ARAPID MEETING ABSTRACTS 2025

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Genetic Mutations, Clinical Features, and Mortality in Severe Combined Immunodeficiency: A Single-Center Experience

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Background: Severe combined immunodeficiency (SCID) is a rare and life-threatening primary immunodeficiency characterized by defective T cell development. SCID results from various genetic mutations, leading to increased susceptibility to severe infections. Early diagnosis and treatment, including hematopoietic stem cell transplantation (HSCT), are crucial for survival.
Methods: A retrospective analysis of patients diagnosed with SCID in pediatric immunology and allergy clinic in Queen Rania Children's Hospital, Amman, Jordan, in the period between 2010 and 2025. Data were collected on age of presentation, diagnostic delays, genetic mutations, clinical features, gender distribution, and mortality; patients with proven genetic test were included. The median and interquartile ranges (IQR) for age at presentation and diagnostic delay were calculated. Additionally, correlations between specific gene mutations and clinical features were analyzed.
Results: 47 patients (25 males, 53%) with proven SCID were included, and the median age at presentation was 3 months (IQR 2-7 months), with a median diagnostic delay of 4 months (IQR 1-16 months). The most common gene mutation was DCLRE1C (17 patients, 36.1%) followed by RAG2 mutation (10 patients, 21.2%) and RAG1 mutation (4 patients, 8.5%). The most common clinical presentation was pneumonia (78.7%), followed by failure to thrive (70.2%) and oral candidiasis (61.7%). DCLRE1C (Artemis) mutation was strongly associated with pneumonia, failure to thrive, and gastrointestinal infections.
Conclusion: SCID remains a devastating disease with significant diagnostic delays and high mortality. DCLRE1C (Artemis) mutation was the most frequently identified. Pneumonia, failure to thrive, and gastrointestinal infections are key clinical markers. Correlations between genetic mutations and clinical features highlight the importance of genetic screening for early diagnosis and timely intervention.

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Inborn Errors of Immunity-Associated Inflammatory Bowel Disease: A Tertiary Center Experience

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Background: Inborn errors of immunity (IEI) are genetic disorders causing immune dysregulation, often increasing susceptibility to infections, autoimmunity, and inflammation. 30% of patients with predominant autoimmune/autoinflammatory IEI present with gastrointestinal symptoms suggestive of inflammatory bowel disease (IBD). IEI-associated inflammatory bowel disease (IEI-IBD) can mimic classic IBD. Treatment for IEI-IBD is not well-established. This study aims to assess the prevalence, clinical and endoscopic presentations, and treatment outcomes of IBD in IEI patients.
Methods: This is a single-center, retrospective study. All patients were ≥14 years of age with a confirmed diagnosis of IEI and IBD based on clinical, endoscopic, and histologic evaluations. Primary outcomes included the prevalence and clinical and endoscopic characteristics. The secondary outcomes included IBD treatment response and safety.
Results: Among 390 patients with IEI, 36 (18.7%) exhibited gastrointestinal symptoms, with diarrhea being the most prevalent symptom (69.3%, n = 25). In the 19 patients who underwent endoscopy, abnormalities were observed in 9 (47.4%), with ulcerations being the most common finding (33.3%). The prevalence of IEI-associated IBD was 2.3% (n = 9), with the most prevalent being CD (55.5%, n = 5), followed by UC and IBD-unclassified (22.2%, n = 2). Family history of IEI was noted in 5 patients (55.5%), while only one (11.1%) had a family history of IBD. Chronic diarrhea (88.9%) was the most common clinical presentation. Initial fecal calprotectin levels were >250 in all patients.

Radiological abnormalities such as strictures, fistulas, perianal disease, and abscesses were reported in 5 patients (55.5%). Medical treatment included corticosteroids in 33.3% (n = 3), immunosuppressants in 22% (n = 2), biologics including vedolizumab, Infliximab, and Adalimumab in 33.3% (n = 3), and 1 patient received no IBD-specific treatment. Clinical response was noted in 3 patients (1 on corticosteroids and 2 on immunosuppressants), with no improvement in those who received biologics. No correlation was found between low baseline lymphocyte marker counts or immunoglobulin levels and lack of clinical response. Surgery related to IBD was required in 2 patients (22.2%).

Conclusion: The prevalence of IEI-IBD in our cohort is low. Characteristics include young age, positive family history of IEI, chronic diarrhea, and abdominal pain. Both intestinal and colonic involvements were noted during endoscopy, with Crohn's disease being the most common IBD subtype. The success of therapy in our cohort was limited and did not correlate with baseline lymphocyte marker counts or immunoglobulin levels. Further investigation involving larger cohorts of patients with IBD, particularly those exhibiting high-risk features (early onset, recurrent infections, and multiple autoimmunities), is necessary to identify individuals with inborn errors of immunity.

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Clinical, Immunological, Genetic Characteristic, and Outcome of Stem Cell Transplantation in ZAP-70 Deficiency: A Single-Center Experience

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Introduction: Zeta chain-associated protein kinase 70 (ZAP-70) deficiency is an exceptionally rare autosomal recessive form of $T^+B^+NK^+$ combined immunodeficiency (CID), associated with a heterogeneous clinical and immunological phenotype. Due to the scarcity of reported cases, outcome data to guide therapeutic strategies, particularly hematopoietic stem cell transplantation (HSCT), are limited. Here, we describe the clinical, immunological, and genetic features, as well as transplantation outcomes and post-HSCT immune reconstitution, in thirteen novel patients managed at a single tertiary care center.

Methods: We retrospectively reviewed clinical, immunologic, genetic characteristics, HSCT outcome, and immune reconstitution for 13 patients who were diagnosed with ZAP-70 deficiency at King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia.

Results: A total of thirteen patients were included, with a mean age at diagnosis of 4 months. The most common initial presentations were recurrent chest infections and skin abnormalities. Autoimmune manifestations and lymphoproliferation were also observed. Immunological evaluation revealed absent or severely reduced CD8+ T cell counts in most patients; however, two patients deviated from this pattern, demonstrating nearly normal CD8+ counts. Three *ZAP-70* mutations in homozygous states were identified. Eleven patients underwent HSCT, with seven from fully matched sibling donors, three from mismatched related donor, and one from umbilical cord. Two patients required a second transplant for poor immune reconstitutions. At last follow-up, eight patients were alive with reasonable immune reconstitution.

Conclusion: Early recognition and timely HSCT are critical for improving outcomes in ZAP-70-deficient patients. Despite challenges in immune reconstitution, mixed lymphoid chimerism was sufficient to achieve clinical stability in the majority of patients.

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Case Report: A Novel Mutation in LAT Gene in an Infant with Severe Combined Immunodeficiency and Hematopoietic Stem Cell Transplantation Outcomes and Literature Review

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Introduction: Linker for activation of T cell (LAT) deficiency is a rare form of severe combined immunodeficiency (SCID), characterized by a disruption in T cell receptor (TCR) signaling, leading to compromised immune responses and immune dysregulation.
Case presentation: We report a 5-year-old Saudi boy, who presented at age 4 months with diarrhea, disseminated Bcgitis, and AIHA. Genetic analysis showed a novel biallelic deletion of the exons 9-11 in LAT gene (c.846-1054cnv), predicted to result in a nonfunctional protein that matches his clinical phenotype. He was also found to have homozygous UNC80 (c.2213G>A) gene mutation, which is related to neurodegenerative disease. He underwent unconditioned FMD HSCT.
Discussion: Our patient underwent unconditioned MSD HSCT to avoid chemotherapy-induced neurotoxicity. STR showed 100% donor lymphoid engraftment at days +30, +90, and +120. He developed acute grade 1/2 GVHD (skin and liver), which resolved with immunosuppression. Currently, he maintains a good quality of life on IVIG, Pentamidine, and Prednisolone. While conditioned HSCT is preferred for long-term immune reconstitution in LAT-related SCID, the associated neurodegenerative disease and risk of BCG reactivation may warrant future consideration of a second HSCT. Literature suggests fully matched transplants improve survival, though long-term outcomes remain unclear due to limited patient data.
Conclusion: Unconditioned MSD HSCT can achieve full donor lymphoid engraftment in LAT-related SCID while minimizing chemotherapy-associated neurotoxicity, though long-term immune reconstitution may require further intervention. More data are needed to assess long-term outcomes, especially in patients with comorbidities and GVHD risk.

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LRBA Deficiency with Metastatic Gastric Cancer: Case Report and Literature Review

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Introduction: Lipopolysaccharide-responsive beige-like anchor protein (LRBA) deficiency is a primary immunodeficiency disorder associated with significant immune dysregulation, recurrent infections, and autoimmunity. While the association between inborn errors of immunity (IEI) and cancer is being increasingly recognized, data on gastric cancers in this context are limited. Here, we present a case of metastatic gastric adenocarcinoma in an LRBA-deficient patient, highlighting the potential oncogenic implications of IEI and reviewing relevant literature.
Case Presentation: A 19-year-old male with LRBA deficiency had a lifelong history of recurrent infections, enteropathy, and severe nutritional and electrolyte deficiencies. Due to the lack of a matched donor, he did not undergo stem cell transplantation, and his family declined treatment with intravenous immunoglobulin and Abatacept. He was diagnosed with metastatic gastric adenocarcinoma at the age of 19. Given his poor performance status and malnutrition, he was deemed unfit for chemotherapy and was transitioned to palliative care. He succumbed to the disease one month after the diagnosis.
Discussion: Gastric cancer incidence in IEI patients is notably higher when compared to the general population. Like many other IEI, cancer link to LRBA deficiency is unproven. To date, only three cases of malignancies in LRBA-deficient patients have been reported—two involving CNS tumors and one with multifocal gastric cancer and melanoma. Our patient is the second documented case of early-onset gastric cancer with LRBA deficiency. Although not fully understood, LRBA dysregulation can impact CTLA4, an immune checkpoint receptor that might be implicated in neoplastic predisposition.
Conclusion: IEI, including LRBA deficiency, should be recognized as a potential risk factor for early-onset gastric malignancies. Larger-scale studies are needed to elucidate underlying mechanisms and improve early detection and management.

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Atypical SCID with RAG2 Mutation: A New Case Report

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Introduction: RAG1 and RAG2 proteins initiate the V(D)J recombination process, enabling the generation of T and B lymphocytes with a diverse repertoire of antigen-specific receptors. Various mutations in the RAG1 and RAG2 genes are implicated in severe combined immunodeficiency (SCID) with variable phenotypic presentations.
Methods: Analysis of clinical and laboratory data and treatment of a child diagnosed with RAG2 deficiency.
Results: A 6-year-old boy, with a family history of a deceased sister at the age of five, was referred to our department for recurrent respiratory infection. He had bilateral subcortical fibrosis with persistent primary vitreous in the right eye. Physical examination revealed facial dysmorphism, depigmented skin lesions, hepatomegaly, and abdominal collateral venous circulation. The patient had anicteric cholestasis with elevated gamma-GT (216 U/L) and liver cytolysis. He was treated with ursodeoxycholic acid and vitamin supplementation, leading to the resolution of liver cytolysis and decreased gamma-GT levels. A biliary MRI suggested early-stage sclerosing cholangitis. Thoracic CT scan showed alveolar consolidations in the lingular and anterobasal segments of the left lower lobe, without bronchial dilatation. Immunoglobulin levels were as follows: IgA <0.2 g/L, IgG 3.04 g/L, and IgM 1.00 g/L. CD markers revealed CD3: 19.5%, CD4: 6%, CD8: 13%, total T cells: 6%, B cells: <0.5%, and NK cells: 78%. Lymphocyte proliferation was reduced in response to both antigens and mitogens. Genetic analysis identified a mutation in the RAG2 gene. The patient experienced recurrent pulmonary and gastrointestinal infections despite regular intravenous immunoglobulin therapy and prophylaxis with itraconazole, cotrimoxazole, and acyclovir. He is currently undergoing preparation for haploidentical stem cells transplantation (HSCT).
Conclusion: RAG2 mutations are the leading cause of T- B- SCID. Certain mutations reduce but do not completely abolish recombination activity, resulting in a milder disease phenotype. Prognosis remains poor in the absence of HSCT.

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Evaluation of Anti-Infective Drug Utilization in Patients with Primary Immunodeficiency at the National Bone Marrow Transplant Center of Tunisia

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Introduction: The National Bone Marrow Transplant Center (CNGMO) in Tunisia provides specialized care for patients with primary immunodeficiency (PID). The management of these patients necessitates the use of high-cost anti-infective agents, warranting a thorough evaluation to optimize budget allocation.
Methods: A retrospective, descriptive study was conducted at the CNGMO, including 21 PID patients, who were admitted for infectious complications and received anti-infective treatments in 2023. Data were extracted from the pharmacy department's drug management software (STKMED) and analyzed using Microsoft Excel.
Results: The total cost of anti-infective agents was fixed at 296,021€. The mean cost per patient was 17,413.03€, SD = 24,474.29€, and costs range from 1,303.78€/patient to 88,586.03€/patient. The most frequently prescribed drugs were Aciclovir and the combination of Sulfamethoxazole + Trimethoprim (71.43%), with costs of 1,794.42€ (112.15€/patient) and 155.65€ (12.97€/patient), respectively. Tazobactam + Piperacillin and Nystatin ranked second (61.9%), with costs of 1,756.6€ (135.12€/patient) and 175.05€ (13.46€/patient), respectively. The most expensive agents were Foscarnet (total of 56,106.12€ and 28,053.06€/patient), Caspofungin (52,968.25€ and 13,242.05€/patient), and Voriconazole (25,940.52€ and 2,594.05€/patient), representing a significant financial burden.
Conclusion: This analysis highlights the substantial economic impact of infections associated with primary immunodeficiency. The high cost of anti-infective treatments reveals the importance of optimized management strategies and enhanced healthcare resource allocation. Establishing an agreement with the national health insurance fund is crucial to ensuring sustainable financial management of the hospital's budget.

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Hematopoietic Stem Cell Transplantation in Chronic Granulomatous Disease: A Single-Center Study

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Introduction: Chronic granulomatous disease (CGD) is a primary immunodeficiency resulting in severe infections and inflammatory complications. Allogeneic hematopoietic cell transplantation (HSCT) restores immune function and improves patient outcomes.
Materials and Methods: This retrospective study included all patients diagnosed with CGD who underwent HSCT at our institution.
Results: This study included 12 CGD patients. Seven received geno-identical transplants and five received haplo-identical transplants. Pretransplant infectious manifestations included pneumonia (n = 11), hepatic abscesses (n = 2), septicemia (n = 5), invasive pulmonary aspergillosis (n = 11), and BCGitis (n = 6). The median age at HSCT was 73 months (SD 45.6), with a range from 11.5 to 164 months, and the median time from diagnosis to HSCT was 40.3 months (SD 35.8), ranging from 3.1 to 140 months. Graft versus host disease was observed in 10 patients, predominantly cutaneous and of grades 1-2. Two patients developed persistent inflammatory colitis; one showed improvement in hemorrhagic rectocolitis, and the other had mild residual congestive rectitis. The overall survival rate at last follow-up was 91.7%. The mortality rate post HSCT was low, with only one patient succumbing to septicemia one month after the procedure. As for post-transplant immune function, the DHR response was observed at 77%, 93%, and 95% in one, one, and three cases, respectively, while two additional tests, lacking DHR results, showed normal NBT test outcomes.
Conclusion: HSCT provided a favorable outcome for most CGD patients, with a low mortality rate and effective management of infections and GVHD. However, persistent inflammatory colitis remains a challenge post-transplant.

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Bone Marrow Transplantation in Severe Combined Immunodeficiencies: What Challenges for the Clinician?

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Introduction: Severe combined immunodeficiencies (SCID) are rare genetic disorders causing immune failure, leading to recurrent, life-threatening infections. Allogeneic hematopoietic stem cell transplantation (HSCT) is the most effective treatment.
Objective: To assess bone marrow transplantation outcomes in children with SCID.
Methods: A retrospective study in the pediatric immunohematology and HSCT unit of the National Bone Marrow Transplant Centre, Tunis, over 18 years (2007–2024). It included patients with SCID who underwent HSCT. Conditioning regimens and complications were defined per 2019 EBMT criteria.
Results: Among 28 patients (14 boys, 14 girls), immunophenotypes were: T-B-NK+ (n = 19), TB+NK+ (n = 7), T-B+NK- (n = 1), and T-B-NK- (n = 1). The median age at diagnosis was 4 months (Q1 = 1, Q3 = 5), and at HSCT, 7 months (Q1 = 3, Q3 = 8). Sixteen had pretransplant infections, including BCGitis (n = 10), CMV (n = 3), RSV (n = 3), and invasive aspergillosis (n = 2). Transplants were genoidentical (n = 8) or haploidentical (n = 20). Conditioning regimen included Busulfan-Fludarabine (n = 17) or Treosulfan-Fludarabine (n = 9), with serotherapy in haploidentical cases (n = 20); two patients had no conditioning. Engraftment occurred in 27 of 28 patients. Mean neutrophil and platelet recovery times were 22 ± 12 days (range: 14–47) and 24.5 ± 12.8 days (range: 7–45), respectively. One child had primary graft failure. Post-transplant complications included acute GvHD (n = 10), hepatic veno-occlusive disease (VOD) (n = 13), viral infections (n = 13; CMV reactivation = 8; viral co-infections = 5), thrombotic microangiopathy (n = 3), BCG reactivation (n = 4), and autoimmune cytopenias (n = 2). After a median follow-up of 2.5 years (Q1 = 1, Q3 = 5), the 5-year survival probability was 65%. Nine early deaths were due to VOD (n = 4), disseminated viral infection (n = 3), thrombotic microangiopathy (n = 1), and septic shock (n = 1).
Conclusion: HSCT outcomes for SCID depend on pretransplant conditions, but toxic and infectious complications remain a challenge. Early diagnosis and avoiding live vaccines are crucial.

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Noninfectious Manifestations in Common Variable Immunodeficiency: A Retrospective Study from a Tunisian Reference Center

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Introduction: Common variable immunodeficiency (CVID) is associated with a broad spectrum of noninfectious manifestations contributing significantly to morbidity. This study describes these complications in CVID patients at a reference center in Tunisia.
Methods: A retrospective and prognostic study was conducted in the Pediatric Immuno-Haematology and Stem Cell Transplantation Department, including patients meeting the ESID criteria for CVID.
Results: Among 36 enrolled patients (16 males, 20 females), noninfectious manifestations were observed in all cases. Gastrointestinal manifestations (n = 27, 75%) included chronic diarrhea (58%), celiac disease (17%), and inflammatory bowel disease (2 cases). Two patients had chronic liver disease, while others had gastroesophageal reflux, enteropathy, intussusception, primary biliary cirrhosis, or cholestasis with biliary cysts (one case each). Autoimmune manifestations occurred in 19 patients (53%), including cytopenias (28%), organ-specific diseases (11%), and systemic diseases (14%) such as lupus (n = 1), myasthenia (n = 1), and rheumatoid arthritis (n = 3). Lymphoproliferation was present in 21 patients (58%), with lymphadenopathy (19%), hepatomegaly (36%), and splenomegaly (36%). Cutaneous manifestations (17%) included pigmentation disorders (n = 3), nodules (n = 1), alopecia (n = 1), psoriasis (n = 1), and allergic urticaria (n = 1). Endocrine disorders affected 28%, including delayed puberty (17%), hypothyroidism (8%), hypoparathyroidism (n = 1), type 1 diabetes (n = 1), and growth retardation (36%). Interstitial lung disease was noted in 11%. Articular manifestations (36%) included arthralgia (n = 10), osteoporosis (n = 5), and lumbar osteoarthritis (n = 1). Neurological disorders (n = 3) included multiple sclerosis (n = 1), epilepsy (n = 1), and autoimmune hypophysitis (n = 1). Malignancies (n = 4) included gastric adenocarcinoma (n = 1), mesothelioma (n = 1), and lymphoma (n = 2).

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Outcomes of Hematopoietic Stem Cell Transplantation in Patients with Hemophagocytic Lymphohistiocytosis Associated with Inborn Errors of Immunity in Tunisia

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Introduction: Hemophagocytic lymphohistiocytosis syndromes (HLH) is one of the warning signs of inborn errors of immunity (IEI) and can be either primary, due to a cytotoxicity defect, or secondary. Hematopoietic stem cell transplantation (HSCT) is a key treatment, particularly for primary HLH.
Objective: To assess HSCT outcomes in patients with IEI-associated HLH at the National Centre for Bone Marrow Transplantation in Tunis.
Methods: This retrospective longitudinal cohort study was conducted in the Pediatric Immuno-Haematology and Haematopoietic Stem Cell Transplant Department in Tunisia over 18 years (2005–2022). It included patients with IEI who developed HLH and underwent HSCT. Conditioning regimen, complications definition, and management were conducted according to the 2019 EBMT definitions.
Results: Thirteen patients underwent HSCT, with a median delay of 4 months (Q1 = 3, Q3 = 4.7) from HLH episode. Nine had primary cytotoxicity defects: FHL (n = 2), immunodeficiency with hypopigmentation (n = 3), EBV susceptibility (n = 2), and unclassified HLH (n = 2). Four had secondary HLH due to other IEIs: ADA2 deficiency (n = 1), CID (n = 1), CGD (n = 1), and LRBA deficiency (n = 1). The transplant was geno-identical in seven cases and haplo-identical in six. Before HSCT, seven patients were in complete remission and five in partial remission. All patients received reduced-intensity conditioning, mainly fludarabine with IV busulfan (67%). GVHD prophylaxis included cyclosporine (n = 13), MMF (n = 6), methotrexate (n = 7) and post-transplant T cell depletion (n = 6). No primary graft rejection occurred.

Neutrophil engraftment was achieved after 25 days (Q1 = 16, Q3 = 28). Post-transplant complications included bacterial (n = 5) and viral (n = 3) infections, acute GVHD (n = 7), and endothelial complications (n = 11). At the last follow-up, 10 patients achieved durable remission, while 3 died from septic shock (n = 2) and severe veno-occlusive disease (n = 1).

Conclusion: Hematopoietic stem cell transplantation is an effective treatment for IEI-associated HLH. It carries risks of infections, GVHD, and endothelial complications. Early identification and timely HSCT are crucial for improving survival in these high-risk patients.

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Predictors of Mortality and Recurrence in Hemophagocytic Lymphohistiocytosis

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Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome characterized by excessive lymphocyte and macrophage activation, leading to immune dysregulation and a cytokine storm. Early identification of factors associated with poor prognosis is essential to improving patient outcomes.

Objective: To identify predictors of mortality and recurrence of HLH in the context of inborn errors of immunity (IEI).

Methods: This retrospective longitudinal cohort study was conducted in the Pediatric Immuno-Haematology and Haematopoietic Stem Cell Transplant Department of the National Bone Marrow Transplant Centre in Tunis over 18 years (2005–2022). It included patients with IEI who developed HLH. Univariate analysis was performed to assess various clinical factors associated with mortality, followed by multivariate analysis using Cox regression to identify independent predictors.

Results: Forty patients were included, 28 with primary HLH (70%) and 12 with secondary HLH (30%). The median age at symptom onset was 4 months (Q1 = 1.2, Q3 = 14.75). Univariate analysis identified several significant predictors of mortality, including age at first symptom ≤10 months (p = 0.01), age at activation diagnosis ≤6 months (p = 0.004), consultation delay >2 months (p = 0.03), clinical anemia with hemoglobin <7 g/dL (p = 0.03), neurological (p = 0.001), hepatic (p = 0.005), or renal (p = 0.02) failure during the first episode of HLH, absence of remission at day 15 (p = 0.01), and familial hemophagocytic lymphohistiocytosis (FHL) (p = 0.001). Multivariate Cox regression analysis identified two independent predictors of mortality: neurological failure (HR = 9.033, p = 0.021, CI [1.388–58.774]) and FHL (HR = 28.064, p = 0.002, CI [3.507–224.542]). HLH recurrence was independently associated with absence of remission within the first 15 days (HR = 4.211, p = 0.004, CI [1.075–23.577]), persistent elevated ferritinemia (HR = 3.848, p = 0.05, CI [1.001–15.218]), and persistent splenomegaly at day 30 (HR = 7.498, p = 0.017, CI [1.431–39.276]).

Conclusion: Neurological failure and FHL are independent risk factors for mortality in patients with IEI and HLH. Early identification and management of these factors are crucial to improving patient outcomes.

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Primary Immunodeficiency and Cancer

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Introduction: Primary immunodeficiency diseases (PID) are caused by inborn errors of the immune system. PID patients with inadequate tumor immunity are at an elevated risk of developing malignancies, such as lymphoma, leukemia, and gastrointestinal cancer.

Methods: Retrospective study of cases of primary immune deficiency (PID), who developed cancer over a period of 37 years (1987-2024) in the Pediatric Immuno-Haematology Department, CNGMO, Tunis.

Results: We collected 11 cases of cancer among 710 patients with PID (1.5%). Patients were distributed as follows: 2/112 cases of ataxia telangiectasia syndrome, 5/49 cases of variable common immune deficiency, one case of LOCID, 1/40 cases of Burton's agammaglobulinemia, 1/30 cases of hyper IgM syndrome, 1/7 cases of severe CD4 lymphopenia, and 1/6 cases of Wiskott-Aldrich syndrome. The mean

age at diagnosis was 5.5 years (2-16 years). The cancers found were as follows: 5 cases of lymphoma, including 2 cases of Hodgkin's lymphoma and 4 cases of malignant non-Hodgkin's lymphoma, 1 case of acute lymphoblastic leukemia, 1 case of Kaposi's sarcoma, 1 case of genital neoplasia, 1 case of bronchoalveolar carcinoma, 1 case of gastric adenocarcinoma, and 1 case of cancer in the head of the pancreas. Death occurred in 8 cases.

Conclusion: After infection, malignancy is the most prevalent cause of death in both children and adults with PIDs.

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The Enigma of Hyper-IgE Syndromes: Is There a Link Between the RAS-MAPK Pathway and STAT6 Activation?

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Introduction: Hyper-IgE syndrome (HIES) encompasses several distinct genetic entities with varying mechanisms and manifestations. Management depends on the specific immune deficiency type, making genetic confirmation essential for guiding therapeutic strategies. Through this case report, authors illustrate the diagnostic challenge of HIES.

Case Report: ST, a 7-year-old boy born to non-consanguineous parents, has presented with severe manifestations since the neonatal period, including allergic symptoms (eczema, food allergy, asthma, urticaria), infectious symptoms (recurrent respiratory and skin infections, oral thrush, with *Staphylococcus aureus* isolated twice), and developmental delay (delayed language acquisition).

Laboratory findings showed eosinophilia (500-1500/mm^3) and elevated IgE levels (1700-2750 IU/mL), while IgG, IgA, and IgM levels, lymphocyte subsets, lymphocyte proliferation assay, phosphorylated STAT3 expression, and vaccine response were all normal. Organ evaluation (abdominal, renal, and cardiac ultrasound, as well as brain MRI) was normal. Chest CT revealed multiple bilateral pulmonary micronodules. Whole-exome sequencing did not detect any phenotype-related variant, except for a heterozygous mutation in the CCDC39 gene (c.2190del p.Glu731Asnfs*31), which is known to cause primary ciliary dyskinesia in a homozygous state. Whole-genome sequencing identified a variant of uncertain significance (VUS) in the LZTR1 gene (c.651G>T p.Glu217Asp), which is associated with RASopathies, including Noonan syndrome and certain myeloid malignancies via RAS-MAPK pathway activation. The RAS-MAPK pathway may modulate STAT6 activity through increased phosphorylation by JAK1 via MEK/ERK → prolonged transcriptional activation and IL-4 production via ERK-mediated transcriptional activation.

Conclusion: This case illustrates the diagnostic challenges of HIES in the absence of a definitive genetic diagnosis and highlights the need for functional validation of VUS. Further research is needed to explore the relationship between RAS-MAPK signaling and immune dysregulation, which could enhance our understanding of hyper-IgE syndromes.

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Evans Syndrome in Children: A Warning Sign of an Inborn Error of Immunity

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Background: Inborn errors of immunity (IEI) are associated with an increased susceptibility to autoimmune diseases, such as autoimmune hemolytic anemia and Evans syndrome (ES).

Objective: To describe the prevalence of IEI in children with ES.

Methods: This was a descriptive and retrospective study conducted in the pediatric immunohematology department in Tunisia over 15 years (2010–2024), including patients diagnosed with ES. Patients with a previously diagnosed IEI before ES onset were excluded. Evans syndrome was defined by the presence of two concomitants or sequential autoimmune cytopenias, and IEI diagnosis followed the 2022 IUIS classification update.

Results: Forty-seven patients (26 boys and 21 girls) were included, with a median age of 39 months (13–81). A confirmed or probable IEI was identified in 35 patients (75%). A family history of hemato-immunologic disorders was present in 15 cases (32%). The first cytopenia was thrombocytopenia (n = 16, 34%), concomitant AIHA and thrombocytopenia (n = 10, 21%), and pancytopenia (n = 6, 13%). Features suggestive of IEI was found in 28 patients (60%), including lymphoproliferation (n = 11), eczema (n = 2), chronic diarrhea (n = 6), recurrent infections (n = 8), and myopathy (n = 1). Most frequently identified IEIs were ALPS (n = 9), LRBA/CTLA4 deficiency (n = 3), SWA (n = 2), ORAI deficiency (n = 1), hyper IgM syndrome (n = 1), common variable immune deficiency (n = 2), LRBA deficiency (n = 2), IPEX syndrome (n = 1), IgM deficiency (n = 1), probable immune dysregulation (n = 9), unclassified IEI (n = 4). Treatment included corticosteroids (n = 47, 100%), intravenous immunoglobulin (n = 16, 34%), immunosuppressive drugs (n = 12), Rapamycin (n = 5), rituximab (n = 1), splenectomy (n = 4), and hematopoietic stem cell transplantation (n = 4). Nine patients died and 39 (83%) experienced relapse during follow-up. Multivariate analysis identified abnormal IgG levels as a predictor of IEI (RR = 21.16, 95% CI [2.5–177], p = 0.005).
Conclusions: The discovery of ES in pediatric patients requires thorough immunological investigations to identify an underlying IEI. Managing ES remains challenging, and treating the underlying IEI can help control the autoimmune process.

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Quality of Life After Hematopoietic Stem Cell Transplantation in Primary Immune Deficiencies

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Background: Hematopoietic stem cell transplantation (HSCT) is a curative treatment in primary immune deficiencies (PID), but at the same time increases the risk of treatment-related morbidity and problems affecting the child's daily functioning. This study aimed to assess the quality of life (QoL) of children with PID after HSCT and to analyze the factors influencing their QoL.
Methods: This was a cross-sectional study, enrolling 25 patients followed after HSCT. The QoL was assessed using two assisted questionnaires for parents and children/adolescents: generic Pediatric Quality of Life (PedsQL 4.0) and the additional PedsQL "stem cell transplant" (SCT) module.
Results: The mean age was 79.73 months ± 60.15 months (10 months-213 months). The overall score for the QoL reported by parents was well correlated with children's responses. The overall QoL after HSCT was lower than the standards defined for healthy subjects. The most affected area after transplant was the academic function having the lowest score. The patient's physical capacity was lower than that of the healthy subjects. The post-transplant emotional state and social relations were not altered with a score close to the norms of healthy subjects. The QoL assessed by the specific SCT module was also satisfactory, with overall parent and patient scores well correlated. Worry problems were most reported by parents and especially those of children under 4 years old. Communication had the lowest score in older children and adolescents. The PedsQL SCT module quality of life score in patients who received a non-myeloablative conditioning regimen was significantly greater than that in patients who had myeloablative treatment (p = 0.008). QoL was better far from HSCT (r = 0.8; p = 0.012).
Conclusions: After HSCT, patients generally do not achieve an especially physical QoL identical to healthy subjects. However, HSCT recipients maintain normal emotional and social functioning. In addition to monitoring physical function and HSCT-related symptoms, monitoring should also consider overall psychosocial functioning. Knowing the factors influencing the quality of life of children receiving HSCT is essential to improve long-term outcomes.

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Evaluation of Healthcare Personnel's Knowledge on the Signs of Inborn Errors of Immunity, Their Management, and Patient Therapeutic Education

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Introduction: The knowledge and competencies of healthcare personnel play a crucial role in managing inborn errors of immunity (IEI). This study aimed to evaluate the knowledge and training needs of healthcare personnel regarding IEI and therapeutic patient education (TPE).

Methods: A cross-sectional study was conducted among healthcare personnel working in the day hospital unit of the pediatric department at National Center for Bone Marrow Transplantation, Tunisia. Data were collected through structured questionnaires containing 25 questions on the clinical manifestations of IEI, treatment options, and the importance of TPE.

Results: The study included 15 healthcare professionals (4 males and 11 females). The mean professional experience at CNGMO was 7.8 ± 5.3 years (range: 1.5–20 years). The median knowledge score was 12/20 (Q1 = 10, Q3 = 16). A significant correlation was found between a score >10 and more than 2 years of experience ($p = 0.044$), as well as the pediatric technician grade ($p < 0.001$). All participants identified recurrent infections as a clinical sign of IEI, and 13/15 recognized growth delay, but only one was aware of the cancer risk associated with IEI. All participants were aware of immunoglobulin therapy; 14/15 knew about antibiotic prophylaxis. Only five understood that bone marrow transplantation is not always indicated.

A significant correlation was found between receiving prior training and a higher knowledge score ($p < 0.001$), better awareness of the role of TPE in preventing bronchiectasis ($p = 0.032$) and reducing healthcare costs ($p=0.01$). Personnel with >2 years of experience demonstrated better knowledge of prenatal diagnosis ($p = 0.038$), cancer risk ($p = 0.040$), and the benefits of TPE ($p < 0.05$).

Conclusion: This study highlights the need for targeted educational programs to improve healthcare personnel's knowledge of IEI. While experience and training positively influence knowledge levels, gaps remain in disease understanding, treatment options, and the role of TPE. Implementing structured training sessions could enhance patient management and overall healthcare outcomes.

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Evaluation of Patients' and Parents' Knowledge of Inborn Errors of Immunity in Children

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Introduction: Inborn errors of immunity (IEI) are chronic conditions requiring complex management. Therapeutic education is essential for optimizing patient care, improving adherence, and preventing complications. This study aimed to assess the level of knowledge patients with IEI have about their disease.

Methods: A descriptive and analytical cross-sectional study was conducted at the Pediatric Department of the National Bone Marrow Transplant Center (CNGMO) in Tunisia. It included 34 patients under 18 years old receiving immunoglobulin replacement therapy. A questionnaire, available in French and Arabic, was administered to parents for children under 10 years (n = 8) and directly to patients aged 10 years or older (n = 26). The questionnaire contained 25 hetero-administered questions covering disease awareness, treatments, adherence, and complications, with scores graded out of 20.

Results: Thirty-four patients (16 boys and 18 girls) were included, with a mean age of 9.3 ± 5.3 years (1-18). The mean follow-up duration at CNGMO was 5 ± 4 years (1-15). IEI types included ataxia-telangiectasia syndrome (n = 4), combined or severe combined immunodeficiency (n = 9), antibody deficiency (n = 20), and Wiskott-Aldrich syndrome (n = 1). The mean knowledge score was 12.16 (range: 8-17). Six patients (17.6%) scored below 10/20, 21 (61.8%), between 10 and 14, and 7 (20.6%) above 14. A significant correlation was found between a score >14/20 and a follow-up duration >1 year ($p = 0.044$). Patients with ataxia-telangiectasia syndrome had significantly lower scores (<10/20), while those with antibody deficiency scored >10/20 ($p = 0.023$). Parents demonstrated significantly better knowledge than patients, particularly regarding treatments, adherence, and complications.

Conclusion: Therapeutic education plays a crucial role in helping patients manage their disease, prevent complications, and improve their quality of life, ultimately fostering autonomy.

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Quality of Life in Patients with Immune Deficiency Receiving Intravenous Immunoglobulin Replacement Therapy

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Introduction: Most primary immunodeficiencies (PID) are characterized by recurrent infections. Evaluating quality of life (QoL) is important for patient care.
Objectives: The main objective was to evaluate the quality of life of children with PID under intravenous replacement infusions of polyvalent immunoglobulins (IVIG). The second objective was to describe the adverse effects associated with IVIG and the social and financial impact of this therapy on families.
Methods: This was a cross-sectional study of forty cases of PID. All immunocompromised patients receiving intravenous replacement immunoglobulins in the Pediatric Department Immuno-Heamatology and Stem Cell Transplant of the National Bone Marrow Transplantation Center in Tunis were enrolled.
Results: The mean age of the patients was 14 years ± 147.36 months (11 months to 47 years). The common variable immune deficiency CVIDs was the most common DIPs in our series (45%). Fourteen (35%) patients have IVIG-related reactions or side effects such as headaches (17%) and fever (10%). This therapy was the cause of school absenteeism in 81.8% of patients and professional absenteeism in 52% of parents. These patients had a reduced quality of life compared to the standards of the healthy subject, mainly for physical health. However, the overall score is not too far from norms, which is probably due to the protective action of IVIG. The emotional and social health of our patients did not differ from healthy controls. The best quality of life score was observed with infants, while the lowest was observed with patients over 18 years of age. Boys had significantly better quality of life than girls. There was no significant correlation between age and type of illness and quality of life. However, high level of residual immunoglobulin G was significantly correlated to better quality of life.
Conclusion: Despite regular immunoglobulin substitutions, the quality of life of these antibody-deficient patients was reduced by standards established for a healthy subject. This quality of life was directly related to the residual IgG level. Adverse events related to IVIG were common but not severe. Moreover, IVIG substitution resulted in additional costs for the family and considerable absenteeism rate. Subcutaneous infusions of immunoglobulins are an alternative that could alleviate these financial and social problems.

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ICF4 Syndrome: From Genetic Diagnosis to Therapeutic Approaches

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Introduction: ICF syndrome (immunodeficiency, centromeric instability, and facial dysmorphism) is a rare genetic disorder characterized by variable combined immunodeficiency and facial anomalies. The ICF4 subtype, associated with HELLS gene mutations, remains poorly described in the literature. We report an illustrative case highlighting the clinical aspects of this syndrome.
Case Report: The patient, the first child of consanguineous parents (second-degree cousins), was born at 39 weeks with facial dysmorphism and growth retardation. During the neonatal period, a congenital cytomegalovirus (CMV) infection was confirmed by a highly positive urinary PCR without detectable visceral involvement, necessitating a 21-day course of ganciclovir treatment. At 4 months, the patient experienced a gastric perforation, leading to peritonitis caused by a non-groupable *Streptococcus*, necessitating surgical intervention. The hospitalization was complicated by severe nosocomial infections, including sepsis with secondary pulmonary involvement. At 8 months, he was admitted to the hospital with severe proctitis, chronic mucoid diarrhea, moderate malnutrition, and delayed growth.

Laboratory tests revealed hypogammaglobulinemia with low levels of IgG, IgA, and IgM. Then, the child developed hepatosplenomegaly, anicteric cholestasis with hepatic cytolysis, and persistent neutropenia. Immunological assessments indicated a severe atypical, combined immunodeficiency, characterized by reduced levels of CD3, CD4, CD8, NK, and B lymphocytes. The NBT test and CD95 expression were within normal ranges, whereas the lymphoblastic transformation response to tuberculin was weak. Genetic testing revealed the diagnosis of ICF4 syndrome. The patient is on regular immunoglobulin infusion with antibiotic, antifungal, and antiviral prophylaxis, showing good progress, adequate weight gain, and no recurrence of severe infectious episodes.

Conclusion: ICF4 syndrome is a rare immunodeficiency disorder with severe clinical manifestations, often requiring hematopoietic stem cell transplantation (HSCT) as a curative option. Advancing genetic research in rare disorders like ICF4 syndrome will enhance early diagnosis, optimize treatment strategies, and improve long-term prognosis.

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Successful Hematopoietic Stem Cell Transplantation in Two Cases of IFNγR1 Receptor Deficiency

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Introduction: Complete interferon gamma 1 receptor deficiency is a rare primary immunodeficiency characterized by increased susceptibility to severe and recurrent mycobacterial infections, as well as other intracellular infections. Treatment with IFN-γ is generally ineffective, with a high rate of early death in infants and young children. Hematopoietic stem cell transplantation (HSCT) could provide the possibility of curative treatment in otherwise refractory cases.

Objective: The aim of this study was to report the results of HSCT for IFNγR1 receptor deficiency.

Methods: A retrospective study including two patients who underwent HSCT for IFNγR1 receptor deficiency.

Results: The first patient was diagnosed at 5 months with BCG disease. The second patient was diagnosed at 10 months with BCG disease. The two patients received an HSCT from a matched related donor at 40 months and 29 months, respectively. Conditioning regimen included fludarabine and Busilvex. GVHD prophylaxis included cyclosporine A and methotrexate. Anti-lymphocyte serum was received by the two patients. Engraftment was achieved in the two cases, BCG disease cured and no GVHD was observed. At last follow-up, they were 12 years old and 3 years old, respectively. They were infection free with a full donor chimerism.

Conclusion: HSCT represents a promising and potentially curative therapeutic alternative for patients with IFNγR1 receptor deficiency. Although this approach is complex and requires rigorous management, it can significantly improve the prognosis of these patients. The reported cases show that BMT can offer a miraculous solution for patients with refractory disease, and we encourage its exploration in other similar settings.

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Vici Syndrome: A Rare Case of Combined Immunodeficiency

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Introduction: Vici syndrome is a rare disorder linked to mutations in the EPG5 gene (18q12.3), which codes for a protein that regulates autophagy. This disease manifests through a range of symptoms, including agenesis of the corpus callosum, brain abnormalities, hypopigmentation, bilateral cataracts, facial malformations and severe immune deficiency, leading to recurrent infections. Around 20 cases have been reported to date. The overall prognosis remains unfavorable, although early identification and proactive management can improve the management of cardiac and immune complications.

Objective: We describe the clinical case of Vici syndrome to highlight the importance of early genetic diagnosis for optimal symptom management.
Results: An 8-month-old full-term infant presented with axial hypotonia, facial dysmorphia (hypertelorism, micrognathism, light hair, ogival palate), poor weight gain, and psychomotor retardation. Repeated episodes of infectious pneumonitis led to a workup for immune deficiency. A genetic study revealed a mutation in the EPG5 gene, confirming the diagnosis of Vici syndrome, associated with a drop in T and NK lymphocytes, suggesting a combined immune deficiency. A chest CT scan showed bronchiectasis of the left lower lobe. Ocular examinations revealed bilateral cataracts, and an echocardiogram revealed no cardiac abnormalities. The patient was treated symptomatically, including regular immunoglobulin infusions, anti-infective prophylaxis, and vitamin supplementation. HSCT was considered, but no match-related donor was available.
Conclusion: This case highlights the importance of early genetic diagnosis in Vici syndrome, allowing more targeted management of immune abnormalities and reducing the risk of serious infections. Although the overall prognosis is poor, proactive management of symptoms, particularly immune deficiency and pulmonary and cardiac complications, can improve the patient's quality of life.

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NFKB1 Mutation and Burkitt Lymphoma: At the Crossroads Between Immunodeficiency and Oncogenesis

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Introduction: Common variable immunodeficiency (CVID) is a primary immunodeficiency disorder characterized by reduced levels of immunoglobulins and impaired antibody responses, leading to recurrent infections, autoimmunity, and an increased risk of malignancies. One of the most well-recognized genetic causes of CVID is mutations in the NFKB1 gene, which plays a crucial role in immune regulation. NFKB1 mutation is associated not only with primary immunodeficiencies (PIDs) but also with an increased risk of lymphoproliferative disorders.
Methods: This case report describes a 16-year-old patient with CVID due to NFKB1 mutation, who later developed Epstein-Barr virus (EBV)-negative Burkitt lymphoma (BL).
Results: The patient was born to non-consanguineous parents of Tunisian origin. Her early childhood was unremarkable until she began experiencing recurrent upper respiratory tract infections associated with hypogammaglobulinemia. Given these findings and a significant family history of primary humoral immunodeficiency, her father having been diagnosed with CVID at the age of 33 and started on immunoglobulin replacement therapy, an underlying immunodeficiency was suspected. Further genetic analysis confirmed a NFKB1 mutation. She was initiated on immunoglobulin replacement therapy along with antibiotic prophylaxis. At the age of 16 years, she developed an aggressive non-EBV-induced Burkitt lymphoma (BL), which was confirmed through histopathology and immunohistochemistry.
Conclusion: This case underscores the complex interplay between genetic immunodeficiencies and oncogenesis, emphasizing the need for vigilant surveillance in patients with CVID. The absence of EBV in this case highlights alternative pathways of lymphomagenesis, particularly in the context of impaired NF-κB signalling. Multidisciplinary management is crucial for early detection and optimal treatment of malignancies in immunodeficient patients.

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Defects in Innate and Intrinsic Immunity in Morocco: Genetic Variants and Their Clinical Impact

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Introduction: Studying innate immune deficiencies is crucial for understanding susceptibility to common infections, as affected patients often have normal immunological profiles yet face diagnostic challenges. This study examines genetic variations in Moroccan patients, emphasizing the need for early detection and treatment.
Method: This is a retrospective study (2008–2024) that analyzed Moroccan IEI registry patients with innate and intrinsic immunodeficiencies, confirmed through CBC, CRP, immunoglobulin levels, lymphocyte subpopulation analysis, and whole-exome sequencing (WES), following the 2022 IUIS classification.
Results: This study highlights the genetic diversity of innate and intrinsic immune deficiencies in Moroccan patients, with Mendelian susceptibility to mycobacterial disease (MSMD) and chronic mucocutaneous candidiasis (CMC) being the most prevalent conditions. Among the 79 patients studied, 46 (58%) had a confirmed genetic diagnosis, with IL12RB1, STAT1, IFNGR1, SPPL2A, TYK2, and TBX21 mutations identified in MSMD cases, and STAT1 and IL17RA mutations linked to CMC. Additionally, three cases of severe viral infection predisposition were linked to a POLR3A, IFIH1, and TLR7XL variation and three cases of bacterial infection predisposition were linked to IRF4, IFNGR1, and NCSTN variation were detected. Notably, a novel IRAK4 mutation (c.277delT, p. F93fsX26) and the SNORA31 variant previously reported in a Saudi Arabian patient were identified. High consanguinity (51.1%) and delayed genetic diagnosis (21–51 months) were observed, emphasizing the need for early genetic screening. These findings underscore the importance of cost-effective diagnostic methods, such as PCR-based genetic screening, to improve early detection and optimize clinical management in Morocco.
Conclusion: This study identifies novel and recurrent mutations in Moroccan patients with innate immune defects, highlighting the high prevalence of MSMD and CMC. The findings underscore the need for early genetic screening to improve disease awareness, early detection, and patient outcomes.

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ZNF341-Related Autosomal Recessive Hyper-IgE Syndrome: A Case Series of Four Patients

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Introduction: Autosomal recessive hyper-IgE syndrome (AR-HIES) caused by ZNF341 deficiency is a rare primary immunodeficiency where the patients displayed combination of high IgE levels, severe dermatitis, skin infections, cold abscesses, recurrent pneumonia, oral thrush, and intellectual disability. Due to its rarity, clinical and immunological characteristics remain poorly understood. We report a series of four genetically confirmed patients with AR-HIES linked to ZNF341 mutations.
Methods: We retrospectively reviewed the clinical, immunological, and genetic profiles of four patients diagnosed with AR-HIES at Mother and Child Hospital El Harrouchi. Diagnosis was confirmed by whole-exome sequencing (WES).
Results: Four genetically confirmed patients with AR-HIES linked to ZNF341 were studied. The age at diagnosis ranged from 3 to 17 years. All patients had elevated IgE levels, with other immunoglobulins normal. Flow cytometry revealed normal CD3, CD4, and CD8 counts, while NK cell levels were low, and PNE levels were elevated in all cases. The clinical manifestations included recurrent skin infections, mucosal candidiasis, and respiratory issues. Some patients had severe forms like necrotizing pneumonia, recurrent impetigo, and otitis. Atopic features such as pruritus, chronic dermatitis, and food allergies were observed. NIH scores ranged from 25 to 51, reflecting clinical severity.
Conclusion: ZNF341-related AR-HIES should be considered in patients with severe eczema, high IgE, and recurrent infections, particularly when STAT3-HIES and AR DOCK8-HIES are excluded. Early genetic testing is crucial for effective management and infection prevention. This case series expands the clinical spectrum of this rare disorder and emphasizes the role of molecular diagnostics in primary immunodeficiencies.

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Exploration of the Clinical and Immunogenetic Profile of Patients with Agammaglobulinemia: About 47 Cases

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Introduction: Agammaglobulinemia is a rare inherited immunodeficiency disorder that is characterized by low (<2%) or absent mature B cells, leading to severe antibody deficiency and a large clinical presentation that varies among patients, such as severe bacterial infections, bronchiectasis, gastrointestinal infections, etc., associated or not with autoimmunity and inflammation. Agammaglobulinemia includes X-linked agammaglobulinemia (XLA), also known as Bruton's disease, which is caused by a mutation in the Bruton tyrosine kinase (BTK) gene, and autosomal recessive or dominant agammaglobulinemia that has been reported to be caused by genes that affect B cells. This study aims to describe the clinical, immunological phenotype, and genetic results of patients with autosomal and X-linked agammaglobulinemia.
Methods: We report 47 patients diagnosed as autosomal or X-linked agammaglobulinemia. Each patient had clinical evaluation, immunological analysis (CBC), lymphocyte subpopulation assay (CD3, CD4, CD8, CD16, and CD19), and immunoglobulin dosage (IgA, IgG, IgM, IgE), and 29 of them also received genetic testing.
Results: 46.8% of the patients had X-linked agammaglobulinemia, while 53.1% had autosomal agammaglobulinemia. The average age at onset of symptoms was 11 months, and the average age at diagnosis was 43.75 months. The sex ratio was 4.87. 23.4% of the patients were born to consanguineous marriages, and 34% had a family history. Clinically, the patients presented with a variety of symptoms, with the most common being sinopulmonary infections (74.5%). Pneumopathy was seen in 42% of patients, gastrointestinal infections in 21%, and skin infections in 42.5%. Autoimmunity was observed in 8% of the patients. All patients had a low (<1%) or absent circulating B cell count, along with significantly reduced immunoglobulin levels. The average levels were 0.08 for IgA, 0.21 for IgM, and 0.77 for IgG. Genetic analysis of the 29 patients identified mutations in the BTK gene in 25 cases, while 3 patients had mutations in the IGHM gene. Additionally, 1 patient carried a double heterozygous pathogenic mutation in the SLC39A gene.
Conclusion: Although the percentage of autosomal agammaglobulinemia is generally low worldwide, in North African countries, it increases due to the high rate of consanguinity. Early identification and diagnosis of agammaglobulinemia is important in decreasing morbidity and mortality, as swift initiation of immunoglobulin replacement may help to prevent sequelae, such as life-threatening infections.

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Complement Deficiencies in Morocco: 6 Confirmed Cases and Variants

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Introduction: Complement deficiencies (CD) are immune disorders where certain complement system proteins are absent or dysfunctional. They are often linked to recurrent invasive infections, renal diseases, and autoimmune conditions. In Morocco, these deficiencies are not well known. This study aims to identify Moroccan patients with CD, diagnosed locally or reported in the international literature.
Methods: Data were collected from the Moroccan PID registry, Moroccan published cases, and patients who underwent genetic testing.
Results: Among the 831 patients registered in the Moroccan Primary Immunodeficiency Registry, only 7 had CD (2 patients with C5 deficiency, 1 with C7 deficiency, 1 with C4 deficiency, 1 with C8b deficiency, 1 with C6 deficiency, and 1 with C3 deficiency). In the

literature, 3 patients with C5 deficiency and 3 with C7 deficiency were identified. Additionally, out of 300 genetically tested patients, 85 had homozygous and heterozygous variants in different complement fractions.

Conclusion: CD do exist in Morocco due to the population's high rate of consanguinity, which also explains the high prevalence of variants related to the disorder. The need to improve awareness and diagnosis of CD is crucial in order to prevent severe complications and enhance the quality of life.

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Poikiloderma with Neutropenia: About Seven Cases

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Introduction: Poikiloderma with neutropenia is an autosomal recessive genetic disorder characterized by poikiloderma and chronic, noncyclic neutropenia. It is often associated with recurrent respiratory tract infections, typically occurring in the first two years of life. Since 2010, mutations in the USB1 gene (C16orf57) have been identified as the cause of this disease. The study aims to raise awareness of this rare condition and promote early diagnosis to prevent complications.

Results: This study reports seven cases, the first four of which were diagnosed in Morocco. All patients presented with poikiloderma, palmoplantar keratoderma, pachyonychia, and neutropenia, accompanied by recurrent infections. Homozygous mutations in the USB1 gene were found in six of the cases, while the investigation of the last case is still ongoing.

Conclusion: Although rare, poikiloderma with neutropenia is an important condition to consider in the differential diagnosis, despite the challenges in recognizing it. Early diagnosis is crucial for ensuring proper follow-up and preventing complications.

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Diagnostic of Chronic Granulomatous Disease: Experience of Ibn Rochd University Hospital

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Background: Chronic granulomatous disease (CGD) is a rare primary immunodeficiency caused by a dysfunction of the NADPH oxidase enzyme, especially in neutrophils (PNN). This defect leads to insufficient production of reactive oxygen species (ROS), which are essential for eliminating intracellular pathogens, thereby predisposing patients to recurrent and severe infections. The dihydrorhodamine (DHR) flow cytometry assay is a functional test used to evaluate neutrophil oxidative activity. This study aims to identify CGD cases in children with recurrent infections and screen carrier females using the DHR test.

Methods: This was a retrospective descriptive study conducted over 24 months in the immunology laboratory at Ibn Rochd University Hospital in Casablanca. Included were patients who underwent the DHR test, while uninterpretable results and incomplete records were excluded. Flow cytometry using DHR with PMA stimulation was used to measure DHR oxidation into fluorescent rhodamine. Data were collected from the laboratory information system and medical records.

Results: The study included 171 patients (58.48% male, 41.52% female), with an average age of 4 years in children and 30.8 years in adults. Most cases came from pediatric departments (161 patients). The main indications were abscesses (32.52%) and recurrent infections (22.76%). The DHR test showed normal neutrophil responses in 135 patients (93.69% PMA response), decreased response in 23 patients (65.76%), and absent response in 13 patients (0.27%). CGD was genetically confirmed in all children with absent oxidative response and in 23.8% of children with a partial response. Two women were identified as X-linked carriers based on the bimodal histogram patterns.

Conclusion: The high proportion of children (94.15%) in this study is consistent with the literature, where 80–90% of CGD cases are diagnosed before the age of five. The DHR test is a rapid and sensitive tool for diagnosing CGD, effectively distinguishing between normal and defective responses. In our series, CGD was confirmed in 100% of children with absent DHR responses, justifying early intervention and family screening.

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Allogeneic Hematopoietic Stem Cell Transplantation for Primary Immunodeficiencies in Morocco

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Introduction: The allogeneic hematopoietic stem cell transplant represents the true curative treatment for several types of primary immunodeficiency or primary immune deficiency disorders. This therapeutic approach allows for the reconstitution of the immune system and helps control infections through the introduction of memory T cells.
Study: We conducted a retrospective study, reporting on 13 cases of hematopoietic stem cell transplants performed in various bone marrow transplant units for children with primary immune deficiencies, followed up in the primary immunodeficiency unit of the Pediatrics 1 department at the Children's Hospital of Casablanca over a period from 2010 to 2024. The aim of our study is to explore the indications, methods and procedures, results, and complications in our series and then compare them with the data and recent series in international literature.
Results: The indication for hematopoietic stem cell transplant was severe combined immunodeficiency in 10 cases, HLA class II deficiency in 2 cases, and combined primary immunodeficiency in 1 case. The average age of our patients at the time of transplantation was 32 months. Add the average transplant delay. In 8 cases, the donor was a fully matched sibling, and in 5 cases, a haploidentical parent. The graft source was marrow in all cases. Eight patients received conditioning, compared to 5 who did not. Graft-versus-host disease prophylaxis was administered in 9 patients in our series, using ciclosporin in all cases, combined with mycophenolate mofetil in 3 cases or with methotrexate in another case. Only three patients developed acute graft-versus-host disease. The outcome was favorable, with stable and satisfactory immune reconstitution in 10 patients. Two deaths were reported after a median delay of 27 days post-transplant, in the context of sepsis. Finally, one patient experienced graft loss 10 years after the transplant, and a second transplant is being considered.
Conclusion: Overall, while our series is limited, the results obtained are very promising. Comparison with results from other series shows many similarities and alignments in terms of outcomes, although efforts are still needed to improve transplant timing, treatment accessibility, as well as follow-up methods, especially chimerism. The therapeutic achievement remains the successful execution of haploidentical transplants, which offer a potential donor for each patient.

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Dermatomyositis: A Single Entity, Mosaic Phenotypes

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Introduction: Dermatomyositis (DM) is an idiopathic inflammatory myopathy with heterogeneous clinical manifestations. Cutaneous symptoms may or may not parallel myositis severity. Advances in myositis-specific antibodies (MSA) have refined DM diagnosis, correlating distinct subtypes with systemic involvement and malignancy risk. This study aims to highlight MSA profiles in DM.
Patients and Methods: A retrospective descriptive study included 12 patients diagnosed with DM at Cheikh Khalifa Hospital and Mohammed VI University Hospital in Bouskoura.

Results: Among 12 patients (66.66% female, mean age 54 years), clinical manifestations were dominated by cutaneous signs (diffuse facial erythema, shawl sign, mechanic's hands, Gottron's papules) and proximal muscle weakness. MSA distribution: anti-Mi2 (5), anti-MDA5 (3), anti-TIF1γ (1), anti-KU (1), anti-Mi2 + anti-TIF1γ (1), inclusion myositis (1), anti-SRP, anti-MDA5 with antisynthetase syndrome. Clinical correlations: anti-Mi2: high CK levels, good prognosis, and low cancer risk. Anti-MDA5: associated with rapidly progressive interstitial lung disease (1 fatal case). Anti-TIF1γ: severe cutaneous lesions, high malignancy risk. Inclusion myositis: poor prognosis (1 fatal case). Treatment involved corticosteroids, methotrexate, and IV immunoglobulins in severe cases.
Conclusion: The identification of MSA subtypes has revolutionized DM classification, improving diagnosis, prognosis, and treatment strategies.

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Multifocal Tuberculosis in the Immunocompromised: About 30 Cases

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Introduction: Immunocompromised conditions give tuberculosis a new dimension, with the emergence of disseminated or multifocal forms. Relatively frequent localizations affect both young adults and the elderly. The prognosis is poor, with mortality remaining high.
Methods: This is a retrospective study of 30 cases of multifocal tuberculosis in patients hospitalized from January 2017 to April 2025 at the respiratory diseases department of CHU Ibn Rochd in Casablanca.
Results: The mean age was 31 years. There were 26 men and 4 women. A history of pulmonary tuberculosis and tuberculosis infection were found in 30% and 41.5% of cases, respectively. Tuberculosis affected two organs in the majority of cases (25 cases), three organs in 4 cases, and four organs in 1 case. HIV-immunocompromised patients accounted for 48% of cases. Diagnosis of tuberculosis was certain in 90% of cases. Bacilloscopy was positive in 45% of cases, and GenXpert in pleural fluid and sputum was positive in 51% and 53.5% of cases, respectively, isolating rifampicin-susceptible *M. tuberculosis*. Patients were treated according to tuberculosis category, as recommended by Morocco's national tuberculosis control program. Short-term outcome was favorable in 21 cases. Death occurred in 9 cases (30%).
Conclusion: Multifocal tuberculosis is often perceived as the prerogative of immunocompromised subjects. It is a preoccupation of respiratory departments in tuberculosis-endemic countries. It remains a serious disease, with a high mortality rate. It is therefore essential to identify the initial infection.

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Variation of HLA-DR Expression in Patients with HLA Class II Deficiency: A Retrospective Study at Ibn Rochd University Hospital

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Introduction: HLA class II deficiency is a rare autosomal recessive primary immunodeficiency characterized by the absence of HLA class II molecule expression on immune cells. This defect impairs cellular and humoral immune responses, leading to increased susceptibility to severe recurrent infections. Diagnosis relies on flow cytometry, which can detect the absence of HLA-DR expression on B lymphocytes. This study aimed to evaluate variations in HLA-DR expression among patients with HLA class II deficiency at Ibn Rochd University Hospital.

Methods: A retrospective study was conducted over four years (January 2021–March 2025) to analyze HLA-DR expression in patients suspected of immunodeficiency. Data were collected from the immuno-serology laboratory. HLA-DR expression on B lymphocytes was measured using flow cytometry after incubation with specific antibodies and erythrocyte lysis. HLA class II deficiency was defined as an expression level below 5%.
Results: Among 426 patients analyzed, 6 (1.40%) had reduced HLA-DR expression. Four patients had expression levels below 5%, consistent with HLA class II deficiency. Two patients had residual levels of 10% and 14%, suggesting a partial defect that may still impair immune function. The average patient age was 11.33 ± 13.8 years, with a male-to-female ratio of 1.94.
Conclusion: The two patients with residual HLA-DR expression highlight the phenotypic variability of HLA class II deficiency. Such cases have been described in the literature, with some studies that suggesting that residual expression may be associated with a distinct clinical phenotype. It is possible that these cases have a different genetic origin, as mutations in regulatory genes like CIITA, RFX5, and RFXAP. Further genetic analysis is needed to clarify the molecular mechanisms underlying partial expression. The predominance of this condition in pediatric populations underscores the importance of early diagnosis and intervention. In Maghreb contexts, pediatricians should consider this diagnosis in the presence of severe recurrent respiratory and digestive tract infections.

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Lymphocytophagy Is a Serious Complication of Severe Combined Immunodeficiency

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Introduction: Lymphocytic erythrophagocytosis is caused by excessive secretion of cytokines by overproliferated lymphocytes leading to phagocytosis of erythrocytes by histiocytes. This serious disease is a rare and fatal complication in patients with severe combined immunodeficiency and usually follows a septic condition in these patients. The aim of the research is to highlight the severity of this complication and raise awareness.
Methodology: This is a 6-year descriptive retrospective study. The inclusion criteria are age group less than 2 years and patients with severe combined immunodeficiency disease with a biological diagnosis of lymphophagy. The study includes the results of clinical examination, biological and septic analyses, and therapeutic parameters.
Results: We studied 8 cases of severe combined immunodeficiency with lymphocytic phagocytosis out of more than 120 cases of severe combined immunodeficiency. The age of the patients ranged from 3 to 13 months, with an average of 6 months, and the sex of the patients was 5 males and 3 females. 4 out of 8 cases had splenomegaly, 4 had hepatomegaly, and 4 had nodules, and all cases had fever during hospitalization. Six cases had pulmonary sepsis, of which 3 had cytomegalovirus isolation, 4 had ear, nose, and throat sepsis, and 1 had urinary sepsis. The most important biological data confirm the collapse of antibody levels in most patients and the diagnostic criteria for lymphocyte phagocytosis were met. In terms of treatment, all patients received antibiotics, corticosteroids in 5 patients, antibodies in 7 patients, and immunosuppressants in 5 patients. All cases died despite receiving treatment.
Conclusion: Co-immunodeficiency disease is a serious disease, and its most serious complication is lymphocytic phagocytosis, which should be searched for in sepsis and during hospitalization, in addition to raising awareness about it because it is rare.

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Emerging Trends and Research Hotspots in Inborn Error of Immunity: A Bibliometric Perspective

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Background: Inborn errors of immunity (IEI) (previously known as primary immunodeficiency) are genetically defined immune disorders that have seen accelerated growth in both research and clinical attention. The genomic era and evolving classification frameworks have transformed the field, making it necessary to map its development, key contributors, and thematic shifts.

Objective: To conduct a bibliometric analysis of global IEI research from 1995 to 2025, identifying emerging trends, influential authors, key institutions, and gaps in regional representation.

Methods: A literature search was conducted using the Web of Science Core Collection (WoSCC) and PubMed databases, limited to English-language publications between 1995 and 2025. Search terms included combinations of genetic- and immune-related keywords such as "monogenic disorder," "gene mutation," "SCID," "PID," and "inborn errors of immunity." After applying defined inclusion and exclusion criteria, a total of 840 original research articles were selected from an initial 1,236. Bibliometric mapping and visualization were performed using Bibliometrix via Shiny in R Studio and VOSviewer to analyze co-authorship networks, keyword co-occurrence, and thematic evolution.

Results: IEI-related publications have increased steadily, with an annual growth rate of 4.5% and a notable surge between 2020 and 2023. The United States, Iran, France, and Germany emerged as leading contributors, with high-impact institutions such as the NIH, Harvard University, and Université Paris Cité playing prominent roles. Among Islamic and Arabic countries, Iran and Turkey demonstrated increasing publication activity, though overall citation impact remained relatively low. Kuwait stood out with a higher average citation rate (23.8), indicating strong influence despite a smaller volume of output. An overlay visualization of international co-authorship networks confirmed the dominance of the United States and Western Europe as central hubs. However, countries like Saudi Arabia, Kuwait, Morocco, and Iran showed a rise in research participation and collaboration since 2018, reflecting growing engagement from several Islamic and Arabic nations, particularly through partnerships with European institutions.

Thematic mapping revealed newborn screening and hematopoietic stem cell transplantation as central, well-developed motor themes, reflecting their critical and evolving role in the field. Foundational but less developed topics included common variable immunodeficiency, whole-exome sequencing, and genetic diagnostics, indicating their broad relevance yet ongoing maturation. Notably, post-2018 research trends demonstrated a pronounced shift toward precision diagnostics, highlighted by the growing prominence of next-generation sequencing and other genomic technologies.

Conclusion: Over the past three decades, IEI research has undergone a transformative shift from phenotype-based classification to genomics-driven approaches, mirrored by the increasing integration of precision diagnostics and translational priorities such as newborn screening and hematopoietic stem cell transplantation, now identified as active and well-developed motor themes. Thematic mapping confirmed the centrality of these evolving domains while also highlighting common variable immunodeficiency (CVID) and whole-exome sequencing as foundational but less developed areas, underscoring ongoing gaps in their clinical translation and research density. Despite substantial progress, disparities in research output and visibility persist across regions. While institutions in established research hubs continue to lead global collaborations, a notable rise in contributions from Arabic and Islamic countries signals a meaningful shift. These emerging efforts are particularly valuable for uncovering underrepresented IEI subtypes linked to consanguinity and region-specific genetic profiles, addressing critical gaps in both global datasets and regional clinical relevance. Sustaining this momentum demands targeted investment in diagnostic infrastructure, inclusive research policies, and equitable collaboration frameworks. Broadening participation from underrepresented regions is not only a matter of global equity but a necessary step toward capturing the full spectrum of IEI diversity.