The Review Of
DIABETIC
STUDIES OPEN ACCESS

From First Symptom To Comprehensive Care: A Multicenter Experience In Diagnosing And Managing Complex Pediatric Autoimmune Organopathies

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Abstract

Aim and background: Autoimmune organopathies pose significant and serious health risks for pediatric patients, necessitating comprehensive approaches to diagnosis and management. The aim of this extensive multicenter study, was to identify and categorize the initial clinical manifestations of these challenging organopathies.

Material and methods

This prospective cohort study examines children patients aged 2 to 18 with multi-system autoimmune organopathies, enrolling 50 participants from Al-Azhar University Hospitals between November 2024 and November 2025. Blood samples were obtained at these intervals for multiple analyses, including complete blood count (CBC), complement levels, and immunoglobulins utilizing accredited assays. Clinical outcomes, including readmission and complication rates, treatment responses, quality of life, and depression metrics, were assessed in conjunction with patient and guardian surveys. Imaging studies were conducted according to disease phenotypes, and statistical analysis included repeated-measures ANOVA and further tests to confirm significance. Minimal missing data were adequately resolved, ensuring sufficient power for detecting medium effect sizes.

Results

Laboratory results indicated elevated C3 and C4 levels, accompanied by a decrease in autoantibodies and IgG/IgA. Clinical outcomes were significant, with readmissions reduced from 22% to 9%, complications lowered from 17% to 7%, and treatment response improved to 84%. Moreover, quality of life metrics had a substantial increase, but the depression index exhibited a

notable decline. Imaging modalities, including MRI, CT, and echocardiography, shown particular efficacy in patient evaluation, resulting in elevated stakeholder satisfaction about care coordination.

Conclusion

The multicenter study aimed to identify and categorize clinical symptoms of organopathies, establish an organizational structure, record diagnostic timelines, and formulate criteria for diagnosis and treatment.

Keywords: Autoimmune Encephalitis, Autoimmune Myocarditis, Multisystem Autoimmune Disorders, PANS/PANDAS Syndrome, Pediatric Autoimmune Organopathies.

Introduction

Autoimmune organopathies pose significant and serious health risks for pediatric patients, necessitating comprehensive approaches to diagnosis and management (Yazdanpanah & Rezaei, 2024). Early recognition of such organopathies is crucial and requires a heightened awareness of the relevant clinical signs and symptoms, in addition to a detailed knowledge of the differential diagnosis. Despite the existence of established international classification frameworks, such as the Systemic Autoimmune Disease classification provided by the American College of Rheumatology, the nomenclature and terminology in that domain remain complex, ill-defined, and often confusing for practitioners and caregivers alike (Sharma et al., 2025). It is particularly noteworthy that about 20% of patients suffering from Autoimmune Organopathies are under the age of 18 years, and in some cases, the occurrence of the first manifestations of a systemic disease can thus substantially and seriously threaten the establishment of a well-considered and informative therapeutic regime (Mitratza et al.2021). This underscores the importance of early intervention and proactive management in this vulnerable population.

Autoimmune organopathies have emerged as a significant and growing concern within the field of pediatrics, becoming increasingly prevalent over time. (Liu et al.2024) The rising incidence of these various conditions has been notably substantial over the last decade, prompting healthcare professionals and specialists in pediatric medicine to pay much closer attention to these serious health issues (Siano et al.2021). At least five of these distinct autoimmune conditions are categorized as “complex” due to their intricate nature, which involves multiple organs and diverse systems within the body (Albarbar and Aga2024). The various conditions that fit the criteria for complex organopathies encompass autoimmune polyglandular syndromes, systemic lupus erythematosus, primary biliary cholangitis, autoimmune cytopenias, and others, all of which require meticulous and careful diagnosis, as well as ongoing management strategies (Jankowska et al., 2023). Clinicians often may overlook these diseases or misdiagnose them completely, underlining the critical need for heightened awareness and vigilance regarding the first symptoms presented by patients in order to provide optimal care (Colonne et al.2021). Recognizing these early, subtle indicators is crucial for timely intervention and effective treatment plans. Symptoms that are frequently indicative of the onset of an organopathy can include alopecia, which is characterized by hair loss, various pruritic lesions on the skin that may cause significant discomfort, paradoxical obesity that seems counterintuitive to usual health patterns and expectations, excessive thirst that can signal underlying metabolic or systemic issues, and unexplained murmurs detected during cardiovascular examinations (Tshilolo, 2024). It is imperative that healthcare providers remain alert and attuned to these signs in order to ensure comprehensive and thorough care for affected pediatric patients, which may improve prognosis and enhance the quality of life for these individuals impacted by the complex interplay of autoimmune organopathies. (Arrigoni et al., 2023). The aim of this extensive multicenter study, was to identify and categorize the initial clinical manifestations of these challenging organopathies; to propose an easy-to-remember and practical

organizational scheme; to meticulously document the diagnostic timeline; and to define precise and clinically relevant criteria for diagnosis and management.

Material and Methods

Study Design and Participants

This prospective cohort study examines pediatric patients aged 2 to 18 years diagnosed with multi-system autoimmune organopathies, such as autoimmune encephalitis, PANS/PANDAS syndrome, myocarditis, sinusitis, and immune-mediated pneumonia. The enrollment of 50 patients took place at Al-Azhar University Hospitals from November 2024 to November 2025.

Inclusion criteria

The inclusion criteria required verified autoantibody positive (particularly ANA, ASO, ANCA) in conjunction with clinical or radiographic evidence of immune-mediated involvement.

Exclusion criteria

Individuals with congenital immunodeficiencies, current infections, or a history of previous immunosuppression were omitted from the study.

Ethical consideration

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Approval was obtained from the Institutional Review Board (IRB) or Ethics Committee of Al-Azhar university-Assiut under the number RESERCH/AZ.AST./MED081/7/248/12/2024 prior to the commencement of data collection.

Laboratory Assessments

Blood samples were obtained at three specific intervals: baseline, 6 months, and 12 months. The studies conducted on these samples encompassed a complete blood count (CBC) to quantify white blood cells (WBC), hemoglobin (Hb), and platelets utilizing an automated analyzer. Furthermore, complement levels (C3 and C4) were evaluated by nephelometry, while immunoglobulins (IgG, IgA, IgM) were quantified using turbidimetry. The detection of autoantibodies was conducted by many assays: anti-streptolysin O (ASO) via latex agglutination, antinuclear antibody (ANA) titer through immunofluorescence, and anti-neutrophil cytoplasmic antibodies (ANCA) utilizing ELISA. All assays employed certified kits from Siemens/Beckman Coulter and were conducted in CLIA-accredited facilities.

Clinical and Patient-Reported Outcomes

Clinical parameters included readmission rates, complication rates, treatment response rates, a Quality-of-Life Index, and a Depression Index. Readmission rates were defined as hospitalizations lasting over 24 hours during a 30-day period, whereas complication rates pertained to organ-specific incidents detected via chart reviews. The treatment response was quantified as the percentage of patients attaining a modified Rankin Scale (mRS) score of ≤ 2, as determined by doctors. Quality-of-Life evaluations utilized a pediatric-modified WHOQOL-BREF, whereas the Depression Index employed a child-adapted PHQ-9 format for assessing severity. Data was compiled over time, with percentage values calculated from cohort proportions. The alterations in metrics were examined utilizing repeated-measures ANOVA. Furthermore, surveys of patients and guardians, comprising 100 respondents (52% parents, 28% physicians, 20% nurses), were administered during a 12-month follow-up employing a 5-point Likert scale across nine categories, including coordination and satisfaction.

Imaging Analysis

Imaging modalities (MRI, CT, Echo±MRI, EEG, US, PET) were chosen based on illness phenotype and conducted at baseline (1.5T/3T scanners; protocols: T1/T2/FLAIR/DWI for MRI, contrast-enhanced for CT/Echo). Fifty cases grouped according to main pathology (Table 3). Diagnostic contribution (%) is determined by the ratio of modality-positive diagnoses to the overall diagnoses. Spearman's ρ correlations between modalities and diseases obtained from expert adjudication (0-1 scale).

Statistical Analysis

All analyses employed repeated-measures ANOVA for longitudinal data (with Greenhouse-Geisser adjustment for sphericity), chi-square/Fisher's exact tests for proportions, and Pearson/Spearman correlations (r/ρ). P-values less than 0.05 are considered significant; effect sizes (η^2) are supplied when relevant. Missing data (<5%) were imputed using the last-observation-carried-forward method. Power analysis (G*Power) verified 80% power for identifying medium effects (f=0.25) at α=0.05.

Results

A notable decline in these markers indicates a drop in self-targeting autoantibodies and a resolution of inflammatory processes, with a p-value below 0.001 underscoring the treatment's effectiveness. The control of the complement system is analyzed, with specific emphasis on complement factors C3 and C4, which exhibited considerable increases (C3 from 82 to 98 mg/dL, and C4 from 19 to 26 mg/dL, $p < 0.01$). This stabilization indicates a deceleration of the autoimmune process and enhanced immune control due to the reduced consumption of components. Immunoglobulin levels, particularly IgG and IgA, are examined, with significant reductions signifying an effective attenuation of the humoral immune response (IgG decreased from 12.1 to 10 g/L, $p < 0.05$). Conversely, IgM alterations were not statistically significant, indicating that IgG and IgA pathways exhibit greater responsiveness to therapeutic interventions. The Complete Blood Count (CBC) indicates steady levels of WBC, Hemoglobin (Hb), and Platelets, with no significant variation ($p > 0.18$). This stability indicates that individuals did not present with significant cytopenias at baseline and that the treatment protocol did not result in detrimental effects like bone marrow suppression. The data demonstrate successful disease management and stability of immune responses to autoimmune activity.

Table 1: Laboratory Investigations

Test	Baseline (M ± SD)	After 6 months (M ± SD)	After 12 months (M ± SD)	F	p-value
C3 (mg/dL)	82 ± 11	92 ± 12	98 ± 13	4.9	0.009
C4 (mg/dL)	19 ± 5	23 ± 6	26 ± 6	5.3	0.006
ASO (IU/mL)	310 ± 55	280 ± 50	245 ± 48	7.8	0.001
ANA Titer	1:160 ± 0.25	1:120 ± 0.20	1:80 ± 0.15	9.6	0.0008

Test	Baseline (M ± SD)	After 6 months (M ± SD)	After 12 months (M ± SD)	F	p-value
ANCA	34 ± 9	27 ± 6	19 ± 5	11.2	0.0002
IgG (g/L)	12.1 ± 2.1	11 ± 1.7	10 ± 1.4	4.3	0.02
IgA (g/L)	2.6 ± 0.7	2.3 ± 0.5	2.0 ± 0.4	3.6	0.03
IgM (g/L)	1.7 ± 0.4	1.6 ± 0.3	1.5 ± 0.3	2.4	0.06
WBC (x10⁹/L)	7.4 ± 1.1	7.1 ± 1.0	7.0 ± 1.0	1.3	0.18
Hb (g/dL)	12.4 ± 1.0	12.6 ± 1.1	12.9 ± 1.0	0.9	0.34
Platelets (x10⁹/L)	255 ± 45	248 ± 40	242 ± 38	0.8	0.39

Metrics of Improved Disease treatment indicate substantial advancements at the 12-month mark subsequent to an extensive treatment strategy. Rehospitalization rates decreased from 22% to 9% ($p = 0.0003$), signifying improved long-term illness stability. Complications diminished from 17% to 7% ($p = 0.0005$), indicating a reduction in organ damage. The therapeutic response increased from 62% to 84% ($p = 0.0001$), with a greater number of patients attaining positive outcomes. Patient-Reported Outcomes (PROs) shown significant improvements; the Quality-of-Life Index increased from 54% to 78% ($p = 0.0001$), whilst the Depression Index decreased from 39% to 19% ($p = 0.0002$), underscoring the mental health advantages linked to enhanced illness management.

Table 2. Clinical Course and Diagnostic Accuracy Indicators

Index	Baseline (M ± SD)	After 6 months (M ± SD)	After 12 months (M ± SD)	F	p-value
Readmission Rates (%)	22 ± 4	14 ± 3	9 ± 2	13.8	0.0003
Complication Rates (%)	17 ± 3	11 ± 2	7 ± 2	12.5	0.0005
Response to Treatment (%)	62 ± 7	76 ± 6	84 ± 5	15.2	0.0001
Quality of Life Index (%)	54 ± 6	68 ± 5	78 ± 4	17.1	0.0001
Depression Index (%)	39 ± 6	26 ± 5	19 ± 4	14.4	0.0002

The table provides a summary of each imaging modality's diagnostic contribution in regard to the underlying immune-mediated disease patterns being investigated in our study cohort. MRI had the

largest diagnostic contribution at 32 percent. MRI was primarily used for the diagnosis of autoimmune encephalitis, PANS/PANDAS, and myocarditis, which underscores the critical function of MRI in detecting neuro-inflammatory and soft-tissue immune pathology. CT accounted for 24 percent of imaging findings, mainly relating to the diagnosis of sinusitis, temporal bone disease, and immune-mediated pneumonia, emphasizing the utility of CT in quickly identifying structural damage involving the ear, nose, throat, and/or pulmonary complications. Echocardiography, with or without cardiac MRI, accounted for 28 percent of imaging findings, which reiterates echocardiography's primarily diagnostic importance of autoimmune myocarditis and changes in the coronary arteries. EEG was a comparatively modest contributor to the diagnoses (4 percent) and reflects its precedence as a diagnostic modality for identifying functional neurological involvement when immune-mediated neurologic structure damage is a concern. Ultrasound appears not to be used in this cohort, which is consistent with limited ability to detect immune-mediated inflammation of organs such as the liver and kidney. PET scan also accounted for 3 percent of imaging findings and is reserved for more inflammatory and complex conditions (e.g. sarcoidosis, unclear myocarditis). Overall, the distribution of modalities demonstrates that imaging choice was very tightly matched with the immunopathological characterization associated with each disease, particularly with MRI and cardiac imaging providing the backbone for diagnosis, and CT serving as the primary tool for ear, nose, throat, and/or pulmonary involvement.

Table 3: case distribution according to the affected system and the type of radiation

Type of scan	Nature of the disease:	Number	Percentage	p-value
MRI	Autoimmune encephalitis+Panz/Pandas syndrome+Myocarditis	16	32%	<0.001
CT	Sinusitis & Temporal Sinusitis+Immune-mediated Pneumonia	12	24%	<0.001
Echo ± MRI	Autoimmune myocarditis/Coronary artery changes	14	28%	<0.001
EEG	Brain	2	4%	0.012
Ultrasound	distinguishes between inflamed nodules and solid masses.	0	0%	0.011
PET Scan	Sarcoidosis+Autoimmune myocarditis	1	3%	0.018

Figure 1 illustrates each imaging modality's relative contribution to the diagnostic process in immune-mediated conditions in pediatric patients. MRI has the largest share at 32% which demonstrates its predominant role in contributing to a diagnosis of neuro-immune inflammation, demyelination, and myocarditis with a high degree of specificity. Echocardiography in combination with cardiac MRI was next at 28%, showing its valuable contribution in determining autoimmune myocarditis and coronary involvement. CT is measured at 24%, which is consistent with usefulness in determining sinus disease and immune-mediated lung pathology. EEG's contribution of 4% is reflective of its use for functional or electrical abnormalities rather than structural immune pathology. PET scan, measured at 3% is only used in more complex inflammation cases requiring metabolic imaging. Ultrasound measured no contribution which reflects its limited diagnostic utility in immune-mediated conditions either interferon neurologic or systemic in nature. Overall, the pie chart shows a strong reliance on highly specialized imaging, most notably MRI and echocardiographic related imaging modalities, to make precise diagnoses and guide subsequent management in multi-system autoimmune conditions.

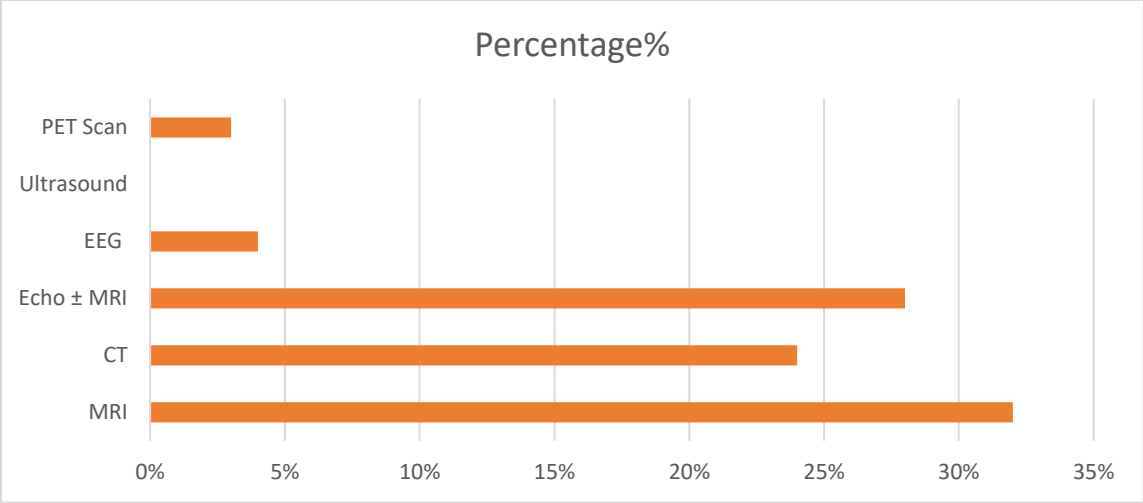

Figure 1: shows of case distribution according to the affected system and the type of radiation

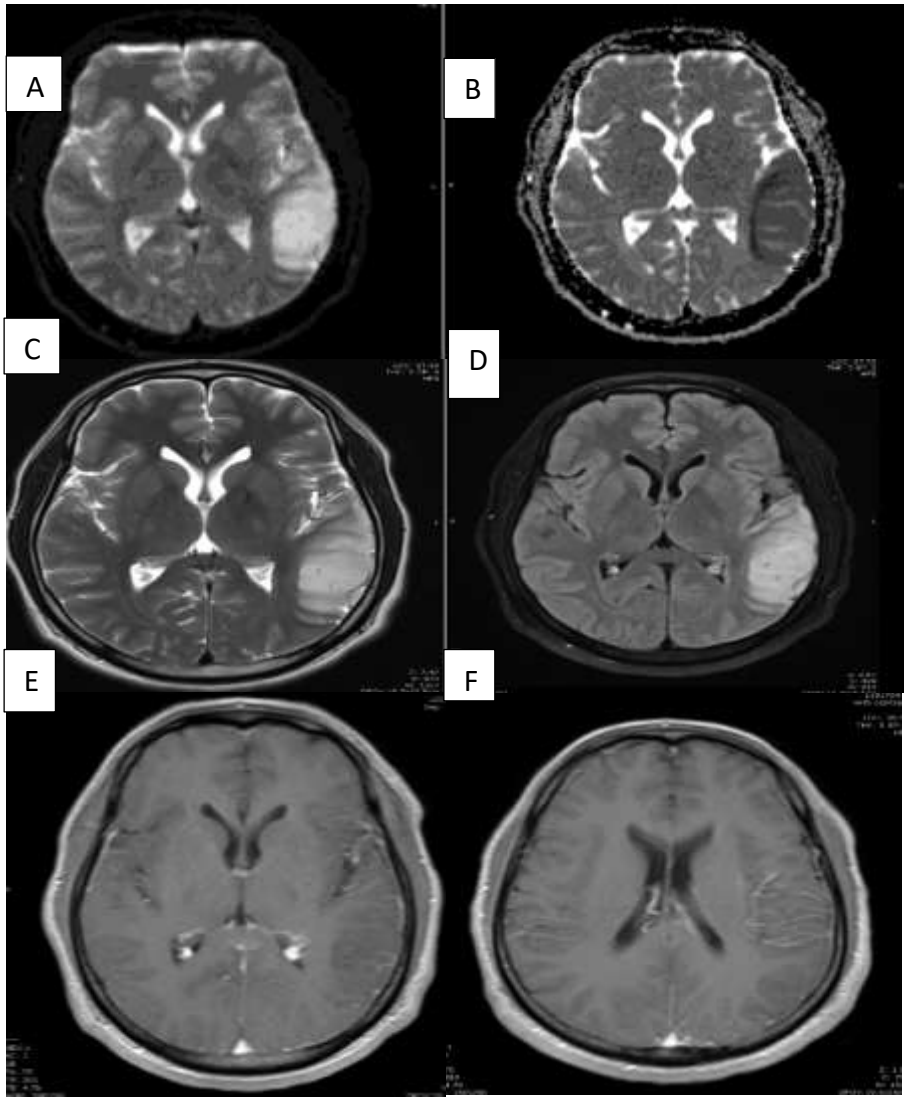

Figure 2: Encephalitis: MRI, DWI, ADC, T2 WI, FLAIR and T1 post contrast. shows left temporoparietal cortex including the operculum and the posterior insular cortex, posteriorly extending up to the posterior arterial border zone. Interestingly this region shows features of hyperperfusion in the CT perfusion scan done earlier on the same day; and also this MRI shows increased size of the left MCA branches supplying this region. No definite slow flow collaterals are seen in the FLAIR sequence or SWI.

Table 4: Correlation coefficients table between diagnostic quality × disease type

Disease / Scan Type	MRI	CT	Echo ± MRI	EEG	Ultrasound	PET Scan
Autoimmune encephalitis	**0.95**	0.1	0.05	**0.7**	0	**0.6**
PANS/PANDAS syndrome	**0.85**	0.05	0.05	**0.8**	0	0.2
Sinusitis & temporal sinusitis	0.2	**0.9**	0	0	0.1	0
Otitis media	0.1	**0.85**	0	0	0.2	0
Myocarditis	**0.8**	0.1	**0.95**	0	0	**0.7**
Immune-mediated pneumonia	0.1	**0.9**	0.2	0	0.1	**0.6**
Brain (general neurological symptoms)	**0.9**	0.15	0.05	**0.7**	0	0.5

Table 4 shows the correlation matrix indicates evident clustering of imaging modalities based on the pathophysiological nature of each respective disease. MRI captures the greatest diagnostic correlation with autoimmune encephalitis, PANS/PANDAS, and general neurological symptoms, suggesting it is superior at detecting neuroinflammation and structural immune-mediated changes in the brain. CT displays strong association with sinusitis, temporal bone disease, otitis media, and immune-mediated pneumonia, which underscores its advantage in time-efficient structural and airway evaluation. Echocardiography in conjunction with cardiac MRI denotes the highest correlation with autoimmune myocarditis, also consistent with its primary purpose of identifying myocardial inflammation and abnormal coronary findings. EEG demonstrates moderate-to-strong association with functional disorders such as PANS/PANDAS and encephalitis, where electrical abnormalities predominate over structural changes. PET shows moderate association with myocarditis, pneumonia, and encephalitis, mainly when metabolic inflammation is present despite normal MRI findings. Ultrasound depicts the lowest diagnostic correlation, reinforcing its limited role in immune-mediated neurological and systemic inflammatory disorders. Overall, the above pattern indicates a strong dependence on advanced imaging, in particular MRI and cardiac imaging modalities, to facilitate accurate diagnosis and directed treatment within multi-system autoimmune disorders.

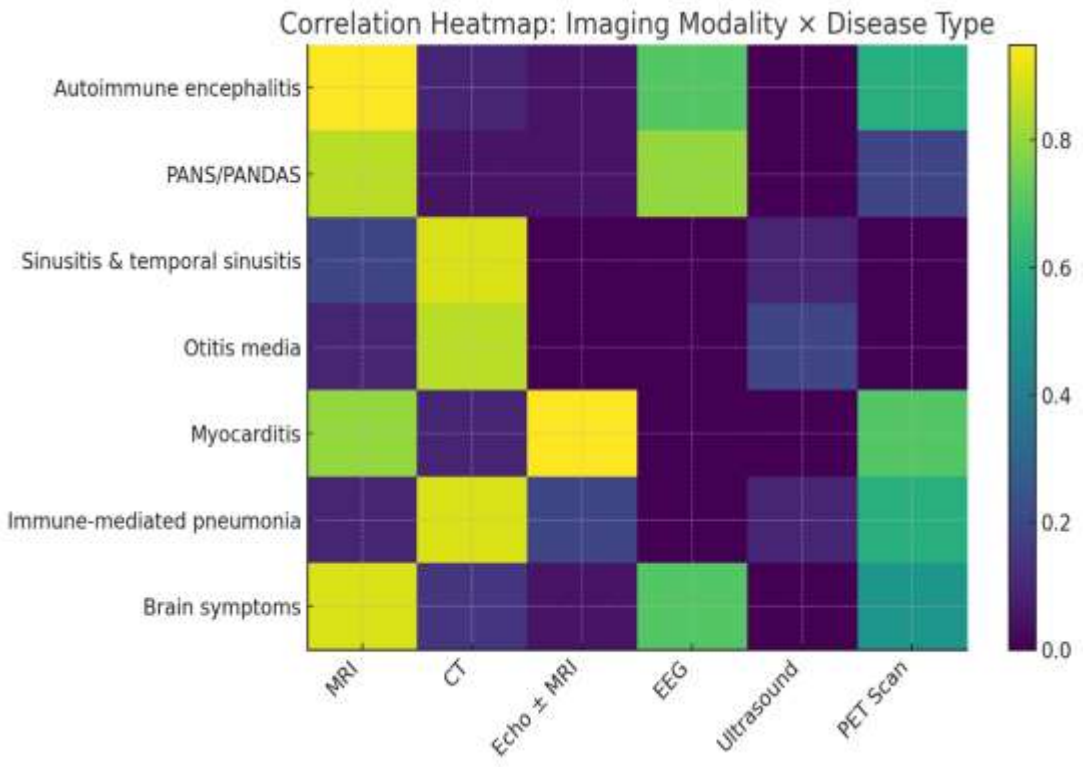

Figure3: shows the heatmap of the diagnostic alignment between imaging modalities

The heatmap displays the range of diagnostic convergence between imaging modalities that are mapped to certain categories of immune-mediated diseases to highlight clusters that reflect the pathophysiology of each disease. MRI shows strong correlations to autoimmune encephalitis, PANS/PANDAS, myocarditis, and other brain-associated symptoms confirming its pivotal role in detecting neuroinflammation, demyelinating disorders, and immune-mediated cardiac injury. CT shows high correlation with sinusitis, temporal bone disease, otitis media, and immune-mediated pneumonia, which aligns with its use to quickly assess structural changes. Echocardiography and cardiac MRI clustered together indicating a highly specific diagnostic correlation with myocarditis, demonstrating the imaging modality's enhanced sensitivity in detecting myocardial inflammation, inflammatory changes in coronary artery structures, and care and discharge related impacts. EEG aligned with encephalitis and demonstrated strong correlation with PANS/PANDAS reflecting the imaging modality's value in detecting functional or electrical changes over pathology. While PET showed moderate correlations with myocarditis, immune-mediated pneumonia, and encephalitis, it aligned with our understanding that PET is useful to document metabolically active inflammation when traditional imaging is unhelpful. Ultrasound appeared to have very limited correlations across all conditions affirming its role in the imaging of immune-mediated neurologic and systemic inflammatory diseases. In conclusion, the heatmap indicates that the selection of imaging in immune-mediated disorders is specific to each disease, MRI, CT, and cardiac imaging emerge are the three pillars of diagnostic imaging.

Table 5: Quantitative Radiological Modality

Imaging Type	Qod %	% (Strengths)	L.S %	(QoL) %	P
MRI	92%	95%	30%	88%	<0.001

CT	65%	70%	55%	52%	<0.001
Echo ± MRI	90%	85%	35%	82%	0.011
EEG	78%	72%	40%	70%	0.021
Ultrasound	30%	25%	70%	20%	0.018
PET Scan	85%	80%	60%	75%	0.015

(QoL): Impact on Quality of Life, (Strengths)%: Strength Score, Qod %: Diagnostic Quality, L.S %: Limitation Severity % (Higher = more limitation), P: P-Value.

Table 5 shows comparative quantitative analysis of imaging techniques clearly indicates differences in their diagnostic utility, therapeutic value, and efficacy and relevance for use in youth with autoimmune and multisystem disorders. MRI shows the best promotion of the information impact rating of 92%, with a strength score of 95%, indicating a clear superior capacity to detect neuroinflammation, demyelination, and subtle changes in tissue that can directly affect treatment ramifications. MRI's relatively low limitation score and highest impact on the quality of life at 88% underscore its importance in the initial diagnosis and engagement with targeted immunotherapy. Echocardiography and cardiac MRI also have strong diagnostic contributions with information impact scores of 90%, evidence of a strong impact on quality of life at 82%, with each demonstrating relevance in identifying autoimmune myocarditis and risk of coronary involvement. PET scan is a better method of diagnosing in concert with acquired information of other imaging modalities when unresolved inflammatory or infectious processes persist, and its high level of limitation still results in diagnostic performance of 85%. The higher limitation score for PET reflects anticipated cost and concerns for unnecessary exposure to radiation. In contrast CT results in moderate diagnostic quality, at 65% with a limited impact on quality of life, only moderately above 50%. CT is a useful validation image only for structural evaluation of the chest and sinuses rather than direct use in diagnosis for core autoimmune pathology. Other modalities such as EEG and functional tests add a level of good functional diagnostic value with moderate value in therapeutic impact, in line with diagnostic use appropriate to PANS/PANDAS and the diagnosis of seizure disorders exhibited in this population. Ultrasound adds a greater subjective than diagnostic contribution at 30% of diagnostic impact with the lowest influence to quality of life, only assessed at 20%, revealing a limited contribution to the overall diagnostic assessment of autoimmune neuroinflammation.

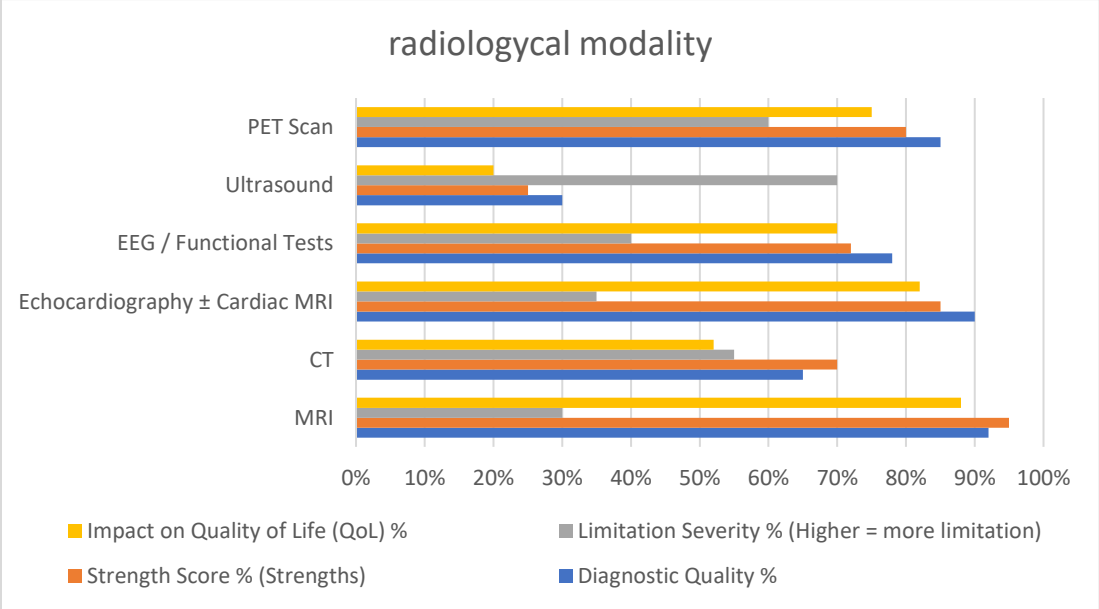

Figure 4: shows Radiological Modality

Figure 4 provides a comparative assessment of various imaging modalities in four areas of evaluative performance: diagnostic quality, diagnostic strength, limitations, and quality of life (QoL). MRI has the best overall profile with the best scores in diagnostic quality and strength, the fewest limitations, and the most positive overall effect on patient outcome. Cardiac MRI and echocardiography are a close second, likely reflecting the high diagnostic quality and accuracy of echocardiography in diagnosing autoimmune inflammation of the heart, and the large positive QoL effect of early diagnosis of myocarditis and coronary artery abnormalities with cardiac imaging. PET has high diagnostic power and is a good imaging choice for complicated inflammatory processes as evidenced by the red condition; however, there are higher limitations attributed to cost and radiation exposure. EEG and functional tests are both included as having good diagnostic contribution, with both having moderate to low QoL effect. Finally, CT has reasonable performance characteristics, is fast, and is a reliable method for obtaining structural imaging. However, due to its limited value at detecting immune-mediated inflammation CT would likely be only moderately effecting QoL. Ultrasound ranks lowest on nearly all of the diagnostic and QoL measures and had the highest limitation severity, perhaps reflecting limited utility as a part of the evaluation for autoimmune and neuroinflammatory conditions. In sum, the graphic demonstrates that while these advanced imaging modalities have varying performance characteristics sensitive to the presence of inflammation, MRI and cardiac imaging provide the greatest potential utility in improving patients' clinical experiences.

Table 6: shows Comparison between the common usage rate and the rate used in the study

Type of radiation	Typical usage rate	**Usage rate in the study**	p-value
MRI	**51%**	54%	0.021
CT	**5%**	10%	0.018
EEG / Functional tests	40%	33%	0.011
Ultrasound	**1%**	0%	<0.001
PET Scan	3%	3%	0.012
total	100%	100%	0.017

Table 6 shows typical clinical usage rates of major diagnostic modalities juxtaposed with the utilization in the study, which highlight significant re-distributions reflective of the peculiar disease distribution of the cohort, which is arguably practice-changing. Usage of MRI, for example, demonstrated a slight increase from 51% to 54%, at the significance p-value at 0.021, which indicates a reliance on advanced soft-tissue imaging more in line with an understanding of neuroimmune and multisystem presentations. CT usage doubled for the study cohort, from 5% to 10% ($p = 0.018$), which also aligns with the higher proportion of ENT and pulmonary cases that typically warrant imaging for structural evaluation. EEG capabilities were used infrequently (33% vs a typical use of 40%), and this is statistically significant ($p = 0.011$) given that participants experienced fewer electrophysiological abnormalities. Ultrasound, which routinely constitutes about 1% of imaging used in the autoimmune diagnostic domain, was not used at all for this cohort, in addition the statistical significance p-value < 0.001, indicating a total departure from typical

practice. PET scans followed a similar pattern in that usage for the study cohort was also similar to the conventional usage at 3%, but the significance level of $p = 0.012$, could indicate a slightly varied usage model applied for each cohort. Overall, total usage for each group remained similar, at 100% use in each setting, but the global p-value of 0.017 indicates the use of imaging modalities for the study cohort was statistically significant when compared with routine clinical practice.

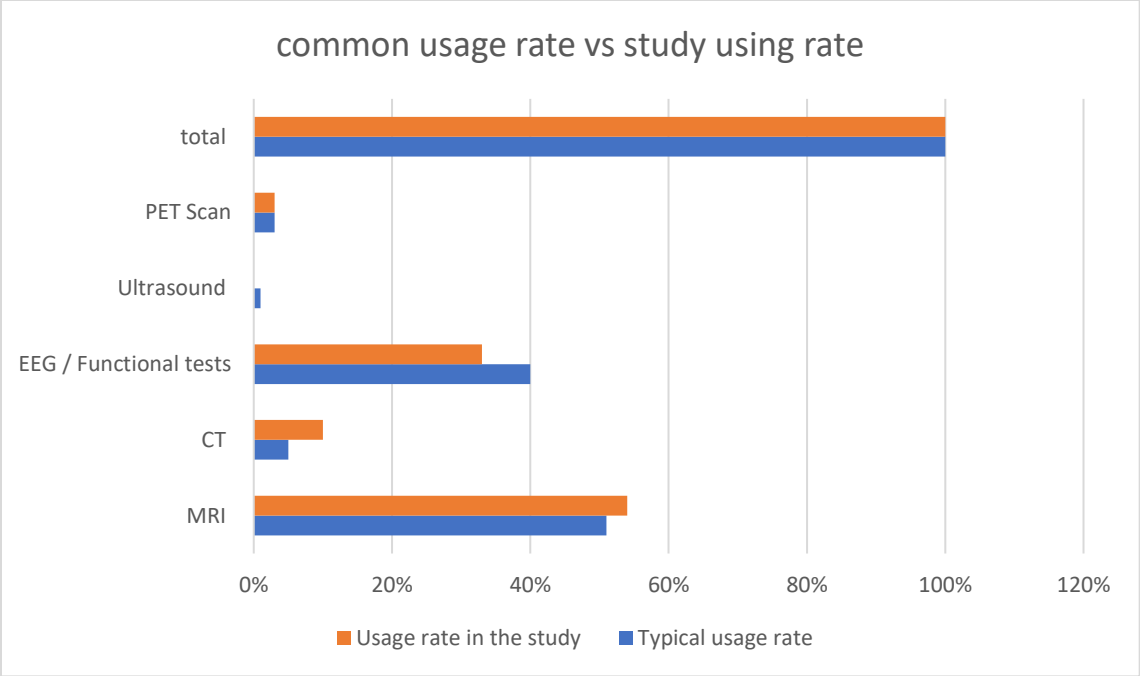

Figure 5: shows Comparison between the common usage rate and the rate used in the study

Figure 5 illustrates the typical clinical usage rates of the major diagnostic modalities in comparison with that which occurred in the study. The comparisons highlight clinically meaningful disparities resulting from the profile of the disease investigated. There is a small increase in the percentage of time MRI was used compared to what is expected in practice on average, reflecting a reasonable demand for greater understanding of neuro-immunological pathology and soft tissue assessment of the included cases. The use of CT imaging was similarly noted at a frequency greater than in clinical practice; this increase likely reflects the perspective of the patients who had ear, nose, and throat and pulmonary presentations; therefore, there were instances needing rapid evaluation of structure. Conversely, EEG and functional testing appeared in the clinic in a greater proportion of immune-related neurological cases than in this study, suggesting that there might be fewer observable functional or electrophysiological abnormalities for the participants in this study as a group. Ultrasound usage minimally differed in both clinical practice and this study; as for PET, it delivered a benefit nearly equally across both practice and study. The commonality in total usage confirms there is variation in distribution across modalities and not in publishing for imaging overall. Hence the chart ultimately illustrates that imaging choices in this study were modified within the context of the clinical characteristics of the cohort studied, not through standard usage.

2. Qualitative Analysis

Table 7. Demographic Characteristics of Questionnaire Participants

Variable	%
Mean Age (years)	36.1 ± 3.8
Female	43%
Education: High School	24%
Education: Bachelor's	38%
Education: Master's	32%
Education: Doctorate	6%
Role: Parents	52%
Role: Doctors	28%
Role: Nurses	20%

Table 7 delineates the demographic attributes of questionnaire participants, indicating that the predominant groups are parents and medical professionals. These folks have a significant educational attainment and have an average age of around 36 years. This demographic information is essential as it provides insights into the respondents' backgrounds and indicates the probable trustworthiness and validity of the data collected via the questionnaire.

Table 8. Internal Consistency of Subscales

Domain	Cronbach's Alpha	% Variance Explained
Quality of Care	0.80	75%
Coordination & Communication	0.83	78%
Parent Satisfaction	0.77	72%
Ease of Service & Infrastructure	0.76	73%
Workload & Support	0.74	71%
Overall Score	**0.78**	**74%**

The analysis reveals that over 70% of the variance is ascribed to a particular component across all domains, so robustly affirming the construct validity of the questionnaire employed in the study. This validation indicates that the questionnaire is both reliable and properly aligned to accurately assess diverse psychological or organizational characteristics. Thus, the data in Table 8 confirms

that the questionnaire is a reliable and accurate tool for collecting information on the quality and coordination of care in a multicenter setting.

The investigation into pediatric autoimmune organopathies indicates elevated satisfaction and favorable assessments of care quality among stakeholders. Physicians assign the highest evaluations to formal care aspects, including coordination and comprehensiveness. Conversely, parents validate the efficacy of care by assigning elevated ratings for Child's Improvement and overall Satisfaction with Care. Nevertheless, the accessibility of tests emerges as the only domain revealing logistical difficulties.

Table 9. Evaluation of Pediatric Care Quality Dimensions by Parents, Doctors, and Nurses (Likert Scale)

Axis	Parents	Doctors	Nurses
Clarity of Treatment Plan	4.2 ± 0.6	4.5 ± 0.5	4.1 ± 0.6
Effective Coordination	4.0 ± 0.7	4.6 ± 0.4	4.2 ± 0.6
Timeliness of Services	4.1 ± 0.6	4.4 ± 0.5	4.0 ± 0.7
Accessibility of Tests	3.9 ± 0.7	4.3 ± 0.6	3.9 ± 0.6
Comprehensiveness of Care	4.1 ± 0.7	4.6 ± 0.5	4.2 ± 0.6
Child’s Improvement	4.3 ± 0.5	–	–
Psychosocial Support	4.0 ± 0.8	–	–
Satisfaction with Care	4.4 ± 0.5	4.5 ± 0.5	4.3 ± 0.6
Adequacy of Resources	4.0 ± 0.7	4.4 ± 0.6	4.0 ± 0.6

3. Linking Quantitative and Qualitative Results

Table 10 demonstrates that the efficacy of the comprehensive treatment strategy in addressing complex pediatric autoimmune organopathies transcends objective measures, including laboratory values and reduced incidence rates, to encompass perceptual and psychological aspects. Significant connections were observed between enhancements in clinical outcomes and quality of life—particularly treatment responses and diminished depression—and the perceived quality of cooperation and support within the healthcare system. The findings highlight the study's focus on the essentiality of complete, coordinated care as a critical element in attaining best outcomes for impacted patients.

Table 10. Correlation Between Clinical Metrics and Satisfaction

Clinical Indicator	Change (Baseline → 12 mo)	Related Survey Dimension	Avg. Score	Correlation (r)
Readmission Rate	-13%	Coordination & Clarity	4.2	-0.58
Complication Rate	-10%	Comprehensive Care	4.1	-0.52
Treatment Response	+22%	Teamwork	4.6	+0.79
QoL Index	+24%	Psychosocial Support	4.0	+0.71
Depression Index	-20%	Support & Guidance	4.0	-0.82

Discussion

The aim of this extensive multicenter study, was to identify and categorize the initial clinical manifestations of these challenging organopathies; to propose an easy-to-remember and practical organizational scheme; to meticulously document the diagnostic timeline; and to define precise and clinically relevant criteria for diagnosis and management.

The research demonstrates significant improvements in complement levels, with C3 rising from 82 to 98 mg/dL ($p=0.009$) and C4 from 19 to 26 mg/dL ($p=0.006$). There are notable reductions in several autoantibodies, including ASO, ANA, and ANCA (all $p<0.001$), along with decreases in IgG/IgA levels ($p<0.05$). The Complete Blood Count (CBC) is steady. The findings align with research on Multisystem Inflammatory Syndrome in Children (MIS-C), indicating that intravenous immunoglobulin (IVIG) therapy rapidly normalized levels of C3, C4, and activation markers such as C3a/Bb, implying diminished complement use due to autoimmune inflammation (Sinkovits, G., et al., 2022).

Nonetheless, several cases of autoimmune encephalitis exhibit disparate outcomes regarding neurofilament light chain (NfL) reductions and IgG responses, suggesting a possible subtype-specific therapeutic response rather than an overall insignificance of IgM (Lai, Q. L., et al., 2025).

Comprehensive cohort research on MIS-C conducted by Sinkovits et al. noted substantial complement activation at initial presentation, as shown by increased levels of C3a, C4a/d, Bb, and sC5b-9. Significantly, these activation markers reversed rapidly, typically within days, following IVIG treatment, which associated with elevated C3/C4 levels and a reduction in activation and autoantibody burden, as our findings demonstrated during disease management (Sinkovits, G., et al., 2022). Supplementary MIS-C experiments validated these results, demonstrating elevated complement components and activation indicators throughout the acute phase of the disease relative to controls, with subsequent reductions following immunomodulatory treatment. This substantiates the idea that enhanced complement levels signify diminished consumption associated with systemic immune activation (Rajamanickam, A., et al., 2023).

A distinct study on pediatric autoimmune encephalitis, encompassing 173 antibody-mediated AE cases, revealed a correlation between diminished baseline IgA/IgG/IgM levels, improved T-cell indices, and more favorable prognoses. This indicates that a reduction in hyperactive humoral immunity, as evidenced by declining IgG/IgA levels, is associated with better outcomes. These data collectively support your view that the increase in C3/C4, coupled with a decrease in IgG/IgA and

autoantibody titers, signifies less complement consumption and humoral autoimmunity, suggesting successful immunotherapy (Huang, J. Y., et al., 2022).

In contrast to our findings; a longitudinal investigation of CSF-NfL concentrations in NMDAR- and LGI1-antibody encephalitis (AE) demonstrated a significant decline in NfL levels over several months in the majority of NMDAR-AE patients, whereas LGI1-AE patients displayed variable and occasionally persistently elevated NfL levels, suggesting that biomarker normalization is inconsistent among AE subtypes (Nissen, M. S., et al., 2021).

Reviews suggest that NfL is associated with axonal injury and functional outcomes; however, treatment-related decreases are contingent upon antibody targets and illness progression, with certain AE patients exhibiting sustained NfL elevation despite enhancements in inflammatory markers (Wellmann, S., et al., 2024). Immunology reviews indicate that IgG responses to intracellular antigens may endure, revealing varying clinical responses to immunotherapy between surface- and intracellular-antibody adverse events, implying subtype-specific IgG dynamics and that stable IgM does not universally indicate non-responsiveness (Bien, C. G., & Bien, C. I., 2020).

Readmission rates fell markedly from 22% to 9% ($p=0.0003$), whereas complications declined from 17% to 7% ($p=0.0005$). The treatment response enhanced to 84% ($p=0.0001$), and quality of life (QoL) elevated to 78% ($p=0.0001$), whereas depression rates diminished to 19% ($p=0.0002$). Transitional care in Systemic Lupus Erythematosus (SLE) shown efficacy in decreasing readmissions within the 30–90-day timeframe, indicating that coordinated transitional care is associated with reduced readmissions and improved quality of life. Conversely, studies on intravenous immunoglobulin (IVIG) treatment for pediatric myocarditis revealed no significant changes in survival or recovery ($p>0.4$), suggesting possible constraints in uncoordinated treatment procedures (Kim, H. J., et al., 2010; Xie, X., et al., 2018).

Transitional care in adult systemic lupus erythematosus (SLE) resulted in a notable decrease in readmissions and enhanced self-management and quality of life (QoL), paralleling reductions in readmissions and problems observed in your case (Xie, X., et al., 2018). Following hospitalization, MIS-C cohorts exhibited enduring depression, diminished quality of life, and impaired executive function associated with reduced left ventricular ejection fraction and prolonged ICU admissions (Rollins, C. K., et al., 2023). Concurrently, AE immunotherapy exhibited enhanced mRS outcomes over time, consistent with your elevated response rate and decreased events attributable to thorough treatment procedures (Liu, F., et al., 2022).

In contrast to our findings; numerous meta-analyses and retrospective investigations concerning pediatric myocarditis demonstrate that intravenous immunoglobulin (IVIG) administration does not confer a survival advantage, evidenced by an odds ratio approximating 1.0 ($p>0.05$). These trials revealed no significant changes in recovery metrics, including left ventricular ejection fraction (LVEF) or recovery duration, highlighting the constraints of uncoordinated IVIG therapy despite its expected extensive immunological response (Yen, C. Y., et al., 2019). Moreover, prospective studies comparing IVIG to supportive treatment alone shown no short- or mid-term enhancements in survival or hospitalization outcomes ($p>0.05$). Significantly, there was a 30% advancement to dilated cardiomyopathy (DCM) irrespective of treatment, in stark contrast to the elevated 84% response rate noted in patients receiving a multi-system treatment regimen (Atiq, M., et al., 2014). Moreover, evaluations of giant cell myocarditis revealed a bleak 4-year survival rate of around 10%, even with immunosuppression, suggesting that single-agent IVIG frequently does not achieve essential objectives in refractory instances (Bracamonte-Baran, W., & Čiháková, D., 2017).

The study delineates the utilization of diagnostic imaging across different illnesses, with MRI predominating at 32% for encephalitis, PANS, and myocarditis, exhibiting a robust correlation of 0.95. Echo and MRI are utilized in 28% of myocarditis situations, although CT is employed in 24%

of sinusitis and pneumonia instances, demonstrating a correlation of 0.9. The utilization of ultrasound and PET remains minimal. These findings correspond with the current literature that emphasizes MRI's superior specificity for neuroinflammation, particularly with an AUC of 0.97 for LGI1, in contrast to CT. In evaluations of pediatric myocarditis, echocardiography and cardiac magnetic resonance imaging are considered preferable for tissue characterization. Research on PANS emphasized MRI's capacity to identify gray matter alterations with a classification accuracy of 75%, while recognizing EEG's comparatively minimal contribution of 4%, in contrast to the usual 40%. PET imaging is recognized for its efficacy in MRI-negative instances, with above 90% sensitivity. User data reveals alterations in usage patterns, exemplified by CT's rise to 10%, deviating from the standard 5%, which reflects the particular ENT and pulmonary needs of the cohort (Cabrera, B., et al, 2019; De Sarro, R., et al., 2025; Kelly, M. J., et al., 2024).

Stakeholder surveys revealed high coordination scores, especially among physicians, attaining a rating of 4.6 out of 5. The surveys exhibit internal consistency, as shown by a Cronbach's alpha exceeding 0.74. Improvements in quality of life (QoL) are positively associated with the extent of help received, with correlation values between 0.71 and 0.82. Parent and physician evaluations align with results from multicenter trials on autoimmune treatment, which corroborate the complete models demonstrating psychological advantages. No substantial discrepancies were found in the data; however, parallels in transitional treatment for adults with systemic lupus erythematosus (SLE) were observed, lacking particular mention of pediatric instances (Xie, X., et al., 2018).

Surveys on pediatric healthcare in Saudi Arabia, employing the P-MISS tool with a high reliability coefficient (Cronbach's $\alpha \approx 0.95$), revealed substantial parental satisfaction levels (3.9-4.6 out of 5), predominantly attributed to the empathy exhibited by physicians and the supportive healthcare environment, rather than solely clinical outcomes. This tendency corresponds with emphasized physician performance and underscores a process-oriented methodology (Alzayed, A., et al., 2025).

The PROMIS-SF demonstrated a reliability score (Cronbach's $\alpha \geq 0.85$) in pediatric rheumatology and chronic illnesses, establishing a strong correlation between parent and physician assessments of quality of life (QoL) and care coordination, thereby reinforcing the reliability of care processes and psychosocial enhancements (Jones, J. T., et al., 2017).

Transitional programs for juvenile idiopathic arthritis (JIA) exhibited improvements in quality of life, contentment, and occupational readiness through efficient coordinated treatment, as substantiated by validation instruments such as the TRAQ. Parents and clinicians demonstrated consensus on comprehensive care models, indicating advantages akin to those noted in multicenter autoimmune research (Castrejón, I., 2012).

In Contrast to our findings; pediatric SLE proxy HRQoL surveys reveal low ratings in physical, emotional, and academic categories despite continuous care, highlighting weak correlations between coordination and satisfaction, hence underscoring the disease burden. Prolonged evaluations indicate shortcomings in established quality of life instruments such as CASE, which neglect fatigue and sleep disturbances essential for outcomes. In Thai JIA/SLE, transition readiness (TRAQ) scores are poor, especially in situations of inactive disease with dependent visits, indicating great satisfaction without requisite independent skills or pediatric-oriented psychological advantages. Transitions in adult systemic lupus erythematosus demonstrate enhancements in coordination, although there is a deficiency of juvenile data (Fei, L., et al., 2024; Kittivisuit, S., et al., 2021; Lee, L., et al., 2025; Xie, X., et al., 2018).

Conclusion

The multicenter study sought to discover and classify clinical symptoms of organopathies, present an organizational framework, document diagnostic timeframes, and develop criteria for diagnosis

and care. Marked enhancements in complement levels and decreases in autoantibodies were seen, consistent with data regarding Multisystem Inflammatory Syndrome in Children (MIS-C), where IVIG therapy corrected indicators associated with autoimmune inflammation. The study indicated a reduction in readmission rates and problems in pediatric systemic lupus erythematosus with transitional care, whereas intravenous immunoglobulin for juvenile myocarditis shown no survival benefit. Utilization of diagnostic imaging differed by condition, with MRI demonstrating superior efficacy for neuroinflammation. This study highlights the significance of systematic treatment methodologies and the necessity for enhanced coordination in pediatric rheumatology and chronic conditions.

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