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Biological Pathways and Biomarker Patterns in Autism Spectrum Disorder: Jalur Biologis dan Pola Biomarker pada Gangguan Spektrum Autisme

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Abstract

General Background Autism spectrum disorder is a complex neurodevelopmental condition characterized by marked heterogeneity in clinical presentation and underlying biology. **Specific Background** Increasing attention has been directed toward biological mechanisms such as immune dysregulation, oxidative stress, mitochondrial dysfunction, and neuroendocrine rhythm disturbances. **Knowledge Gap** Despite extensive research, findings remain fragmented across biological systems, limiting integrative understanding. **Aims** This article aims to synthesize current evidence on key biological pathways and biomarkers associated with autism spectrum disorder. **Results** The review identifies consistent abnormalities in inflammatory markers,oxidative stress indicators,mitochondrial function, melatonin regulation, and serotonergic activity, suggesting interconnected physiological alterations. **Novelty** Thestudy offers an integrative synthesis that brings together immune, metabolic, and neurobiological evidence within a single analytical framework. **Implications** These findings support the relevance of multi-system biological perspectives in autism research and provide a consolidated foundation for future investigations into diagnostic and therapeutic strategies.

Highlights:

-
- Multiple physiological systems show recurrent abnormalities in autism spectrum disorder.
- Immune and oxidative pathways appear closely interconnected across studies.
  Neuroendocrine rhythm disturbances emerge as a consistent biological feature.

Keywords: Autism Spectrum Disorder, Neuroinflammation, Oxidative Stress, Biomarkers, Biological Mechanisms

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Introduction

Autism spectrum disorder (ASD) was a complex neurodevelopmental disorder that was characterized by repetitive behavioral patterns, restricted interests, likewise persistent problems with social communication (1,2). Also , the prevalence of ASD has increased significantly in the past decade thanks to the increased diagnostic awareness and potential genetic and environmental factors (3,4). The increasing of research suggests that ASD was characterized by major physiological, metabolic, and immunological alterations that lead to it was diverse manifestation, in contrast the behavioral aspects of ASD were quite clear (5,6). Moreover , one of the disorders most frequently recorded in ASD was hormonal dysregulation (7). As an example, sleep disorders, impaired circadian rhythms modulation, also, elevated oxidative vulnerability were all associated with melatonin deficit in a number of children with autism, as demonstrated by various studies (8). Nevertheless , another initial biochemical predictor of ASD was high levels of serotonin or hyperserotonemia that influencing neurodevelopment, gastrointestinal, sensory and also, behavioral inflexibility (9,10). So, Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has also been evidenced and increased cortisol response has been observed indicating a change in stress responses and constant physiological alertness (11,12). In addition, oxidative stress has been identified to have significant pathogenesis of ASD (13) . It has been discovered that autistic individuals show a great deal of elevated concentrations of total oxidant status (TOS) and lipid peroxidation product, malondialdehyde (MDA) which were indicative of increased production of reactive oxygen species (ROS) and also impaired redox balance in cells (14). Then ,these oxidative attacks were often accompanied by reductions in antioxidant defenses in the form of glutathione peroxidase (GPx) which was necessary to protect the brain tissue against oxidative damage(15,16). Furthermore , there has been a growing acceptance that dysregulation of the immune system in addition to hormonal and oxidative conditions was one of the core features of ASD (17). So, There was also an increase in pro-inflammatory cytokines such as interleukin-12 (IL-12), interleukin-8 (IL-8), and interleukin-1 β (IL-1 β) in serum, cerebral spinal fluid, and postmortem brain tissues of individuals with ASD (18). ASD neurobiology was believed to have a strong role played by the functions of these cytokines in promoting neuroinflammation, microglial activation, as well as abnormal neuronal connections (19). Thus , ASD pathogenesis was connected, immune activation in the chronic form can increase the severity of oxidative stress and disrupt hormonal mechanisms (20). Consequently , the entire available evidence indicates intricate relationships between oxidative imbalance, inflammatory cues, as well as hormonal disregulation as the source of ASD. So , the simultaneous study of these biomarkers may help to know better the causes of ASD and be more able to locate the objective diagnostic markers. Therefore to provide the light on the possible diagnostic and mechanistic implications of the hormonal, oxidative, and immunological indicators, the given study compares the autistic youngsters with the healthy ones.

Materials and Methods

A. Study Design and Population

A study was carried out between September 2024 up to June 2025 in a groups of privately and neurodevelopmental clinics in the Wasit Province , Iraq. In this study, fifty children with autism spectrum disorder (ASD) and fifty healthy controls were used, whereby they were matched in terms of age and sex. The conventional diagnostic criteria aided in checking all ASD diagnoses with the assistance of the pediatric and behavioral specialists. However , children that had any acute illness, autoimmune diseases, chronic inflammatory diseases as well as genetic syndromes and other neurological malformations were not allowed to participate.

B. Sample Collection and Analysis

In this study five milliliters of venous blood were collected on each of the children. After centrifugation, clotting, and isolation of serum samples was done; serum was stored at -20 C^{o} pending analysis. Cortisol, serotonin and melatonin measured using ELISA kits (Elabscience, China). Also , the biomarkers of oxidative stress TOS were determined with ELISA kit (Elabscience, China; Rel Assay Diagnostics, Turkey) and MDA with a commercial kits MDA ELISA kit (Elabscience, China; MyBioSource, USA). The activity of glutathione peroxidase (GPx) was measured by an enzymatic kinetic kit (Randox, UK). And , immunological markers (IL-1β, IL-12 and IL-12) were determined using Sandwich ELISA kits (Elabscience, China). All the assays were performed according to the instructions of the manufacturer as well as analyzed twice to achieve precision.

C. Statistical Analysis

The data were analyzed on SPSS version 25. Categorical variables were presented in percentages and frequencies, but the quantitative values were presented in mean ± SD. Group differences between children with autism and controls were evaluated using the independent samples t-test . Also , to test the diagnostic performance of IL-1 β, IL-8 and IL-12 in terms of AUC, sensitivity, specificity and ideal cutoff values through ROC curve analysis. Pearson correlation was employed in order to determine correlations between cytokines and oscillators of oxidation/hormone. The significance was considered to be statistically significant with a p-value of less than 0.05.

D. Ethical Approval

The ethical committee of the College of Science of the University of Wasit approved the protocol of the study (Approval No. BIO-2025-012).

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Results and Discussion

A. Results

1. Population Under Examination Characteristics

Table (1) shows the demographics of the patients, as well as the control persons. The age of the children with autism was 5.14±0.81 years, while the average age of the control was 4.64 ± 0.77 years. The two groups had no significant difference (P = 0.172). Also there was no significant difference in the frequency distribution of the patients and control subjects by age group. Nevertheless, the autistic children that took part in the current study were younger than or equivalent to the age of 5 (31(62.0%). Frequency distribution of patients and control subjects between male and female did not differ significantly (P = 0.410), 33 (66.0%) males and 17 (34.0%) females constituted the autistic children and 29 (58.0%) and 21 (42.0%) males and females in the control group, respectively.

Table 1. Characteristics of the Autistic Children and Healthy Control.

Characteristic	**Autistic children (n=50)**	**Healthy Control (n=50)**	***P***
Age (years)	5.14 ± 0.81	4.64 ± 0.77	0.172
Gender			
Male, n(%)	33 (66.0%)	29 (58.0 %)	0.410
Female, n (%)	17 (34.0%)	21 (42.0%)	
Age Groups			
≤ 5 years, *n* (%)	31 (62.0%)	37 (74.0 %)	0.198
6-10 years, *n* (%)	19 (38.0%)	13 (26.0%)	

2. Hormonal Parameters of the Patients and the Controls

In Table (2) The mean levels of Melatonin were significant lower in children with autism (17.78 ± 3.55) compared with control groups (56.51 ± 9.74) .In contrast, the present results show that mean levels of Serotonin in children with autism were significantly greater than in healthy controls (274.86 ± 28.4 versus 135.00 ± 12.7), respectively (P > 0.05). In addition , the mean cortisol levels were significantly higher in autism children than in the healthy controls (P>0.05).

Table 2. Comparison between Hormonal parameters (Melatonin, Serotonin and Cortisol) in Autistic children and healthy controls.

Groups		**Melatonin (pg/ml)**	**Serotonin (ng/ml)**	**Cortisol (µg/dl)**
Autistic children	**Mean ± SD**	**17.78** ± 3.55	**274.86** ± 28.4	**21.13** ± 1.97
	Range	8.00-28.00	197.00-319.00	18.50-24.80
Control	**Mean ± SD**	**56.51** ± 9.74	**135.00** ± 12.7	**11.34** ± 1.40
	Range	36.00-75.00	99.00-176.00	8.50-13.40
p-value		**0.001****	**0.001****	**0.001****

SD: standard deviation; †: Independent T test; **: significant at *P* > 0.05

3. Antioxidant Parameters of Patients and Controls

As in Table (3), the autistic children had a higher level of malondialdehyde (MDA) (5.19 ± 0.61 nmol/ml) as compared to the healthy control group (2.14 ± 0.31 nmol/ml) ; the difference between the two was significant (P=0.001). In addition , the existing results show that mean Total Oxidant Status (TOS) of children with autism was much higher than that of healthy controls (22.53 ± 3.14 µmol versus 11.87 ± 2.09 µmol, correspondingly; P=0.001). Although, the mean value of glutathione peroxidase (GPx) in children with autism was significantly lower as compared to that of healthy children (44.10 ± 4.89 U/L and 69.90 ± 3.10 U/L, respectively).

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Table 3. The an tioxidant parameters (MDA, TOS and GPx) of children with autism and healthy control.

Groups		MDA(nmol/ml)	TOS (µmol)	GPx(U/L)
Autistic children	**Mean ± SD**	**5.19** ± 0.61	**22.53** ± 3.14	**44.10** ± 4.89
	Range	4.10-6.00	18.00-28.90	37.00-59.00
Control	**Mean ± SD**	**2.14** ± 0.31	**11.87** ± 2.09	**69.90** ± 3.10
	Range	1.70-2.80	8.80-15.80	64.00-76.00
p-value		**0.001****	**0.001****	**0.001****

SD: standard deviation; †: Independent T test; **: significant at $P > 0.05$

4. Immunological Parameters of Patients and Controls

Table (4) show there were significant elevated in all immunological parameters (IL-1 β , IL-12 and IL-8)in the children with autism disorder compared with control groups . So , Serum IL-1β mean level in the cases group was 14.12 ± 1.69 pg/ml whereas in the control group was 6.67 ± 1.08 pg/ml. This difference had a statistical significance(P< 0.001). In the same way, serum IL-8 level were markedly increased in autistic children (7.71 ± 1.01 pg/ml) compared to controls (3.29 ± 0.79pg/ml; P= 0.001). And , there was significant increase of IL-12 levels in Autistic children (30.29 ± 3.35 ng/ml) in compared to healthy controls (17.62 ± 4.79 ng/ml; P = 0.001).

Table 4. Comparison of Immunological parameters (IL-1β, IL-8 and IL-12) in Autistic children and healthy controls

Groups		IL-1β (pg/ml)	IL-8 (pg/ml)	IL-12 (ng/ml)
Autistic children	**Mean ± SD**	**14.12** ± 1.69	**7.71** ± 1.01	**30.29** ± 3.35
	Range	11.00-16.80	5.90-9.10	24.71-35.90
Control	**Mean ± SD**	**6.67** ± 1.08	**3.29** ± 0.79	**17.62** ± 4.79
	Range	3.10-12.00	1.10-6.10	8.80-27.00
p-value		**0.001****	**0.001****	**0.001****

SD: standard deviation; †: Independent T test; **: significant at $P > 0.05$

5. Diagnostic Performance of Immunological Parameters (Il-1β, Il-8 and Il-12) in Autistic Children

Receiver operating characteristic (ROC) curve analysis (Table 5) demonstrated excellent diagnostic performance for all Immunological (IL-1β, IL-8 and IL-12) biomarkers. IL-1β showed an optimal cut-off value of >11.70 pg/ml, these biomarker achieved 96.0% sensitivity, 94.0% specificity, 94.1% positive predictive value (PPV), and 95.9% negative predictive value (NPV), with an area under the curve (AUC) of 0.977 (95% CI: 0.949- 1.000; P < 0.001), indicating exellent discriminatory power between Autistic children and healthy controls.

6. Autistic Children Immunological Markers (Il-1 0 Il-8 and Il-12): Diagnostic Performance

All immunological biomarkers (IL-1β, IL-12, and IL-8) had good diagnostic performance demonstrated by receiver operating characteristic (ROC) curve analysis (Table 5). IL-1β had a perfect cut-off value of above 11.70 pg/ml with an area under the curve (AUC) of 0.977 (95% CI: 0.949-1.000; P < 0.001). These biomarkers had a sensitivity of 96.0, specificity of 94.0 and positive predictive value (PPV) and negative predictive value (NPV) of 94.1 and 95.9 between autistic children and healthy controls respectively. Also ,The IL-8 showed outstanding diagnostic properties of autism: cut-off value is less than 6.05 pg/ml, 92.0 sensitivity, 94.0 specificity, 93.9 PPV, and 92.2 NPV and the area under the curve (AUC) is 0.976 (95% CI: 0.948-1.000; P=0.001). Furthermore , IL-12 has great autism diagnostic criteria.

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Table 5. Roc curve of I mmunological M arkers (IL- 1β , IL-8, and IL-12) in children with autism.

Characteristic	IL-1β (pg/ml)	IL-8 (pg/ml)	IL-12 (ng/ml)
Cutoff value	>11.70	**>6.05**	> 25.25
P value	**< 0.001**	**0.001**	**< 0.001**
Sensitivity %	96.0 %	92.0 %	90.0 %
Specificity %	94.0 %	94.0 %	92.0 %
PPV %	94.1 %	93.9 %	91.8 %
NPV %	95.9 %	92.2 %	90.2 %
AUC (95% CI)	0.977 (0.949- 1.000)	0.976 (0.948- 1.000)	0.949 (0.893- 0.990)

CI: Confidence interval, AUC: Area under curve.

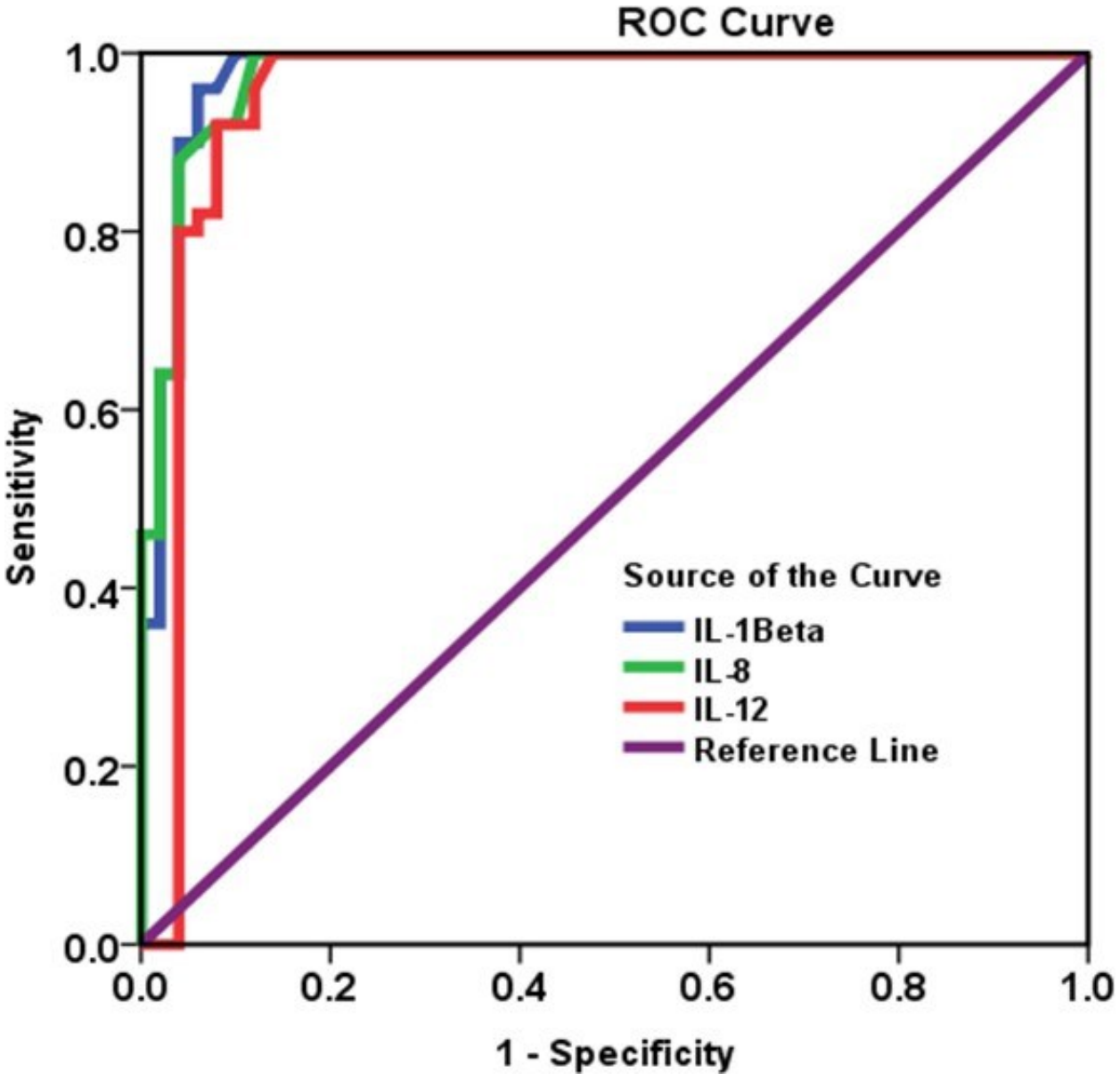

Figure 1. Receiver operating characteristic (ROC) curves of IL-1β (blue), IL-8 (green), and IL-12 (red) levels in differentiating autistic children from healthy controls.

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Figure 1 (Blue curve) Receiver operating characteristic curve of IL-1β levels to differentiate Autistic children and healthy control subjects. (Green curve) IL-8 level receiver operating characteristic curve to differentiate Autistic children and healthy control subjects. (Red curve) Receiver operating characteristic curve of the level of IL-12 to differentiate Autistic kids and healthy control subjects.

7. The Correlation of Immunological Markers (Il-1β, Il-8, and Il-12) and Other Variables in Autism Children

The interacting relationship between IL-1β and cortisol (r=0.459 and p=0.001), IL-8 and IL-12 (r=0.303 and p=0.032) between the IL-12 and TOS (r=0.425 and p=0.001) and the IL-12 and serotonin (r=0.530 and p=0.001) are positive in children with autism. However, IL-1β level and GPx (r=-0.278 and p=0.047), IL-12 level and Melatonin (r=-0.338 and p=0.016) had a significant negative correlation in autistic children. No other parameter did, however, have any significant association.

Table 6. Correlation between Immunological parameters (IL-1β, IL-8 and IL-12) and other parameters in Autistic children. (,n and)

Parameters	Immunological parameters					
	IL-1β (pg/ml)		IL-8 (pg/ml)		IL-12 (ng/ml)	
	r	*P*	*r*	*P*	*r*	*P*
IL-1β	1					
IL-8	0.131	0.365	1			
IL-12	0.142	0.326	0.303	0.032*	1	
MDA	0.025	0.862	0.009	0.951	-0.453	0.001*
TOS	0.261	0.067	0.123	0.394	0.425	0.001*
GPx	-0.278	0.047*	-0.198	0.167	-0.092	0.524
Melatonin	-0.090	0.535	-0.097	0.502	-0.338	0.016*
Serotonin	0.066	0.651	0.253	0.077	0.530	0.001*
Cortisol	0.459	0.001*	0.211	0.141	0.228	0.111

r: correlation coefficient.

B. Discussion

The findings of the present work prove the existing opinion that Autism Spectrum Disorder (ASD) was a systemic neurodevelopmental disorder and not a simple behavioral one as they present solid evidence to support the idea that ASD was associated with combinedhormonal, oxidative, and immunological disruptions (2, 21). As a result , the significantly reduced levels of melatonin in children with autism were in line with a massive amount of evidence which determines that melatonin deficit was among the most common biochemical deviations in ASD (22,23). Due to the importance of melatonin in immunological regulation, circadian rhythms regulation, and antioxidant protection, its deficiency could be related to sleep disorders, increased oxidative stress, also impaired neurodevelopment common in ASD children (24,6). Although, the increased levels of serotonin in the current study give more support to the accepted theory that ASD was linked with hyperserotonemia that has been reported in more than one-third of children with the disorder (9,25). Therefore ,abnormally high peripheral serotonin may be caused by altered transporter action, dysregulated tryptophan metabolism, or a high gut enterochromaffin activity variable related to the above characteristics of behavioral rigidity, sensory abnormalities, and gastrointestinal dysfunction variables (26). Furthermore, the high level of cortisol in children with ASD indicates the impairment of the hypothalamic pituitary adrenal (HPA) axis, consistent with increased stress response of the physiologic form associated with the disorder (11,27). So , Chronic HPA activity was found to correlate with emotional dysregulation, anxiety, and poor social functioning (28).The significant difference of oxidative stress indicators was observed in children with autism where MDA and TOS were higher and GPx was lower(13). Such findings are consistent with the other studies that evidence the existence of oxidative imbalance in the pathogenesis of ASD (29). Thus , the augmented lipid peroxidation and lower antioxidant enzyme functions may aggravate neuroinflammatory reactions, interrupt neuronal signaling and mitochondrial functions (30,31). Since , reduced GPx levels were proposed by impaired glutathione-dependent detoxification processes which have been commonly associated with oxidative disturbance in ASD (32). In this study, the autistic children of the immunological group possessed a higher level of IL-1 β, IL-8, and IL-12, which show great inflammatory stimulation. As a result ,it has been known that high levels of IL-1β inhibit learning, enhance neuroinflammation, and disrupt synaptic

plasticity (17). Moreover , abnormal neuronal growth and synapses architecture were also associated with increased chemotactic signaling and possible activation of microglia suggested by the elevated IL-8 (33). So, IL-12, which was an important Th1 immunological mediator, could be a sign of altered brain immunological-neural interactions as well as suggest systemic immune activation (34). Thus , the growing evidence that neuroinflammation was one of the major causes in ASD was justified by these cytokine abnormalities (20).These cytokine abnormalities have a high AUC value and therefore suggest that they can be used as biomarker candidates. Moreover , prior studies also have demonstrated cytokine panels to be curious predictive and diagnostic exploits of ASD (35). The suggestion of interdependence between immune homeostasis and HPA dysregulation was also justified by the favorable linkage between IL-1 β and cortisol (36). Also , The positive relationship between oxidant state and IL-12, along with the emerging interdependence of oxidative and inflammatory pathways where reactive oxygen species trigger cytokine expression and the reverse is also indicated (37). The anti-inflammatory and antioxidant properties of melatonin are aligned with the reverse relationship that exists between melatonin and the indicators of inflammatory state (38).Ultimately, this evidence indicates that neuroendocrine disorders, oxidative imbalance, and immunological stimulation interact complexly to trigger ASD. Such biological disruptions have the potential to impair the cortical maturation, synaptic connection, and neuronal development which eventually affect the clinical presentation of ASD. The integration of immunological, oxidative, and hormonal biomarkers can enhance the accuracy of diagnosis and early diagnosis and focus the personalized treatment strategies.

Conclusion

The study indicates that children with autism exhibit significant immunological, oxidative and hormonal alterations. Higher levels of serotonin, cortisol, MDA, TOS, IL-1 β, IL-12 and IL-8 while lower levels of melatonin and GPx indicate complex interrelations between neuroendocrine functioning, redox disproportion, as well as inflammatory activity. Thus , the immunological biomarkers, particularly IL-1 β, IL-8 and IL-12, were well diagnostic, and may be used in the screening of ASD. So , these findings reinforce the importance of the integration of biomarker based procedures in diagnosis and treatment interventions and argue in favor of the multi biological nature of ASD.

References

1. D. Skuse, K. Greaves-Lord, G. Rodrigues da Cunha, and G. Baird, “Autism Spectrum Disorder,” The Lancet, vol. 392, no. 10146, pp. 508–520, 2018.
2. J. Zeidan et al., “Global Prevalence of Autism: A Systematic Review Update,” Autism Research, vol. 15, no. 5, pp. 778–790, 2022.
3. M. J. Maenner et al., “Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network,” MMWR Surveillance Summaries, vol. 69, no. 4, pp. 1–12, 2020.
4. K. Lyall et al., “The Changing Epidemiology of Autism Spectrum Disorders,” Annual Review of Public Health, vol. 38, no. 1, pp. 81–102, 2017.
5. R. E. Frye and D. A. Rossignol, “Identification and Treatment of Pathophysiological Comorbidities of Autism Spectrum Disorder,” Clinical Medicine Insights: Pediatrics, vol. 10, pp. 1–13, 2016.
6. A. Masi et al., “Cytokine Aberrations in Autism Spectrum Disorder: A Systematic Review and Meta-Analysis,” Molecular Psychiatry, vol. 20, no. 4, pp. 440–446, 2015.
7. C. Feybesse, S. Chokron, and S. Tordjman, “Melatonin in Neurodevelopmental Disorders,” Antioxidants, vol. 12, no. 11, Art. no. 2017, 2023.
8. S. E. Goldman et al., “Melatonin in Children With Autism Spectrum Disorders: Endogenous and Pharmacokinetic Profiles,” Journal of Autism and Developmental Disorders, vol. 44, no. 10, pp. 2525–2535, 2014.
9. C. L. Muller, A. M. Anacker, and J. Veenstra-VanderWeele, “The Serotonin System in Autism Spectrum Disorder: From Biomarker to Animal Models,” Neuroscience, vol. 321, pp. 24–41, 2016.
10. M. M. Abdi, “Towards Molecular Diagnosis of Autism Spectrum Disorder Using Multi-Omics Approaches,” Ph.D. dissertation, Hamad Bin Khalifa University, Doha, Qatar, 2023.
11. R. A. Muscatello et al., “Physiological Profiles and Depressive Symptoms in Autism Spectrum Disorder,” Journal of Autism and Developmental Disorders, vol. 51, no. 1, pp. 15–29, 2021.
12. B. A. Corbett and D. Simon, “Adolescence, Stress and Cortisol in Autism Spectrum Disorders,” OA Autism, vol. 1, no. 1, Art. no. 2, 2014.
13. G. Bjorklund et al., “Oxidative Stress in Autism Spectrum Disorder,” Molecular Neurobiology, vol. 57, no. 5, pp. 2314–2332, 2020.
14. R. E. Frye et al., “Emerging Biomarkers in Autism Spectrum Disorder,” Annals of Translational Medicine, vol. 7, no. 23, Art. no. 792, 2019.
15. S. J. James et al., “Metabolic Biomarkers of Increased Oxidative Stress and Impaired Methylation Capacity in Children With Autism,” The American Journal of Clinical Nutrition, vol. 80, no. 6, pp. 1611–1617, 2004.
16. A. Aytulun and D. Unal, “Neuroinflammation and Autism,” International Journal of Developmental Disabilities, pp. 1–21, 2024.
17. P. Goines and J. Van de Water, “The Immune System’s Role in the Biology of Autism,” Current Opinion in Neurology, vol. 23, no. 2, pp. 111–117, 2010.
18. J. Mead and P. Ashwood, “Evidence Supporting an Altered Immune Response in ASD,” Immunology Letters, vol. 163, no. 1, pp. 49–55, 2015.
19. J. Prata et al., “The Contribution of Inflammation to Autism Spectrum Disorders,” in Psychiatric Disorders: Methods and Protocols, New York, NY, USA: Springer, 2019, pp. 493–510.
20. M. D. L. A. Robinson-Agramonte et al., “Immune Dysregulation in Autism Spectrum Disorder,” International Journal of Molecular Sciences, vol. 23, no. 6, Art. no. 3033, 2022.
21. C. Lord et al., “Autism Spectrum Disorder,” Nature Reviews Disease Primers, vol. 6, no. 1, Art. no. 5, 2020.
22. S. Tordjman et al., “Autism as a Disorder of Biological and Behavioral Rhythms,” Frontiers in Pediatrics, vol. 3, Art.

no. 1, 2015.
23. A. W. Galion et al., “Practice Pathway for Night Wakings in Children With Autism Spectrum Disorder,” Journal of Autism and Developmental Disorders, vol. 54, no. 8, pp. 2926–2945, 2024.
24. J. Melke et al., “Abnormal Melatonin Synthesis in Autism Spectrum Disorders,” Molecular Psychiatry, vol. 13, no. 1, pp. 90–98, 2008.
25. D. Esposito et al., “Autism and Hyperserotonemia: A Review,” Brain Sciences, vol. 14, no. 5, Art. no. 481, 2024.
26. P. Srikantha and M. H. Mohajeri, “The Possible Role of the Microbiota–Gut–Brain Axis in Autism Spectrum Disorder,” International Journal of Molecular Sciences, vol. 20, no. 9, Art. no. 2115, 2019.
27. A. Niego and A. Benitez-Burraco, “Autism and Williams Syndrome: Molecular and Cognitive Overlaps,” International Journal of Developmental Disabilities, vol. 68, no. 4, pp. 399–415, 2022.
28. E. G. Spratt et al., “Cortisol Response to Stress in Children With Autism,” Journal of Autism and Developmental Disorders, vol. 42, no. 1, pp. 75–81, 2012.
29. R. E. Frye et al., “Biomarkers of Mitochondrial Dysfunction in Autism Spectrum Disorder,” Neurobiology of Disease, vol. 197, Art. no. 106520, 2024.
30. A. Chauhan and V. Chauhan, “Oxidative Stress in Autism,” Pathophysiology, vol. 13, no. 3, pp. 171–181, 2006.
31. P. M. Abruzzo, C. Panisi, and M. Marini, “Alteration of Chloride Homeostasis and GABAergic Signaling in Autism Spectrum Disorders,” Antioxidants, vol. 10, no. 8, Art. no. 1316, 2021.
32. S. L. Burke et al., “Evidence for Oxidative Stress in Autism Spectrum Disorders,” Journal of Autism and Developmental Disorders, vol. 51, no. 5, pp. 1428–1445, 2021.
33. I. Tonhajzerova et al., “Inflammatory Activity in Autism Spectrum Disorder,” in Respiratory Health, Cham, Switzerland: Springer, 2015, pp. 93–98.
34. W. Nour-Eldine et al., “Immune Cellular Sources of Abnormal Cytokines in Autism Spectrum Disorder,” Frontiers in Immunology, vol. 13, Art. no. 950275, 2022.
35. M. Gevezova et al., “Inflammation and Mitochondrial Dysfunction in Autism Spectrum Disorder,” CNS and Neurological Disorders - Drug Targets, vol. 19, no. 5, pp. 320–333, 2020.
36. A. Meltzer and J. Van de Water, “The Role of the Immune System in Autism Spectrum Disorder,” Neuropsychopharmacology, vol. 42, no. 1, pp. 284–298, 2017.
37. X. Liu et al., “Oxidative Stress in Autism Spectrum Disorder: A Meta-Analysis,” Frontiers in Psychiatry, vol. 13, Art. no. 813304, 2022.
38. S. da Silveira Cruz-Machado et al., “Disrupted Nocturnal Melatonin Secretion in Autism Spectrum Disorders,” Journal of Pineal Research, vol. 70, no. 3, Art. no. e12715, 2021.

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