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Diagnostic Potential of Vitamin D, Chromogranin A, Tumor Necrosis Factor-α, and Cortisol Levels in Attention-Deficit/Hyperactivity Disorder: A Meta-Analysis

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Highlights

What are the main findings?

- This meta-analysis demonstrates significantly lower vitamin D, cortisol, and TNF-α levels in individuals with ADHD compared with controls.
- Vitamin D showed the strongest and most consistent association with ADHD across studies.

What are the implications of the main findings?

- Neuroendocrine and inflammatory biomarkers may complement clinical diagnosis and improve biological characterization of ADHD.
- Future standardized longitudinal studies are required to validate these biomarkers for diagnostic and prognostic use.

Abstract

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder that is linked to attention, hyperactivity, and impulse control. There is emerging evidence that markers like Vitamin D, Chromogranin A (CgA), Tumor Necrosis Factor-α (TNF-α), and cortisol can be used to explain its biological mechanisms. **Objective:** To quantify serum levels of Vitamin D, CgA, TNF-α, and cortisol in ADHD patients and control subjects, and establish their diagnostic value. **Methods:** According to PRISMA guidelines, we searched Google Scholar and PubMed systematically for observational studies that assess the serum levels of the selected biomarkers in ADHD and control groups. The studies that passed the inclusion criteria were screened, extracted, and analyzed using a random-effects model. The effect sizes were presented as Hedges' g. Heterogeneity was assessed using I^2 statistics, and potential publication bias was assessed using funnel plots and Egger's test. Meta-regression was conducted to explore moderators like age, gender, and comorbidities. **Results:** 28 studies were included. Vitamin D was significantly lower in ADHD patients compared to controls (SMD = -1.19, 95% CI: -2.04 to -0.33, p = 0.0068), but heterogeneity was high (I^2 = 96.5%). TNF-α was significantly lower (SMD = -0.39, 95% CI: -0.65 to -0.13, p = 0.0033) with low heterogeneity (I^2 = 22.0%). Cortisol was significantly lower (SMD = -0.78, 95% CI: -1.48 to -0.08, p = 0.0280), with high heterogeneity (I^2 = 94.3%). Chromogranin A results were inconclusive due to limited data. Meta-regression revealed that age, male sex, and comorbidities significantly moderated Vitamin D effect sizes, but other predictors were not significant. **Conclusion**: Vitamin D, TNF-α, and cortisol are all greatly diminished in ADHD and are potential additional diagnostic markers. CgA is worthy of further study.

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1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a very common neurodevelopmental disorder globally, with typical symptoms of inattention, hyperactivity, and impulsivity, and with important influences on academic, social, and emotional functioning [1,2]. According to the Global Burden of Disease (GBD) 2019 study, the age-standardized global prevalence of ADHD is estimated at 1.13% (95% UI: 0.831–1.494) across all ages, with the highest prevalence observed in the 10–14 years age group and the highest incidence in the 5–9 years age group [3]. A comprehensive meta-analysis of epidemiological studies, however, suggests that the true global prevalence among children and adolescents is approximately 7.2%, which highlights a benchmark for understanding diagnostic trends [4].

Furthermore, epidemiological studies indicate that ADHD occurs among 5–7% of school children worldwide [5]. In India, where the studies are more sporadic, the prevalence is highly variable, depending on diagnostic criteria, sampling design, and cultural factors [6]. In one study, the prevalence was found to be 6%, with a higher prevalence in boys and those with poorer socioeconomic status [7]. In contrast, in Nigeria, the prevalence among adolescents was 8.8%, with subtypes including 3.08% inattentive, 2.05% hyperactive-impulsive, and 3.08% combined type [8].

ADHD is also more prevalent in men than in women. Research suggests that rates are twice as high in men globally [9]. Despite being ubiquitous, underdiagnosis is a significant issue. This is also seen in women, teenagers, and in low- and middle-income countries [10–12]. Further, ADHD often persists into adulthood. Rates from 2.5% to 6.8% have been found, depending on whether child-onset persisting or symptomatic adult ADHD is included [13].

Genetic and environmental factors are well-established causes of ADHD. More recent data have also implicated biochemical and neuroinflammatory markers in the causation of ADHD. These markers include dysregulation of neuroendocrine systems and immune response. For example, elevated pro-inflammatory cytokines, such as TNF-α, and neuropeptide markers [14,15]. Hypovitaminosis D and abnormal cortisol levels have also been implicated. These factors affect stress and arousal systems and may connect with ADHD symptomatology [16]. The evidence is highly variable. A systematic evaluation is necessary to confirm these biochemical markers in ADHD [17].

Hence, in the current meta-analysis, an effort is made to systematically compare the standardized mean differences between Vitamin D serum levels, TNF-α, cortisol, and CgA levels in ADHD patients compared to normal controls. Through a synthesis of the available literature, this research aims to clarify the biochemical correlates of ADHD and contribute to its neurobiological foundation, which could yield biomarker-based data for both diagnosis and therapeutic monitoring.

2. Materials and Methods

2.1. Hypothesis

There are significant differences in the serum levels of Vitamin D, Chromogranin A (CgA), Tumor Necrosis Factor-alpha (TNF-α), and cortisol between ADHD patients and non-ADHD controls, suggesting their diagnostic potential.

2.2. Objectives

- To determine if each biomarker (Vitamin D, Chromogranin A (CgA), TNF-α, and cortisol) shows statistically significant mean differences between the ADHD and control groups.
- To assess the potential diagnostic value of Vitamin D, Chromogranin A (CgA), TNF-α, and cortisol for ADHD.

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- To explore the consistency of findings for Vitamin D, Chromogranin A (CgA), TNF-α, and cortisol across studies and populations.

2.3. Search Strategy

This meta-analysis was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Literature search was conducted using two major electronic databases: PubMed and Google Scholar, covering all years up to the most recent available date.

To ensure comprehensive coverage, the following keywords and logical operators were used to form the search string:

The search string used the following keywords and logical operators: The search string was structured as follows, using logical operators and parentheses to ensure correct groupings: ("attention deficit hyperactivity disorder" OR ADHD) AND (("Vitamin D" OR "25(OH)D" OR "25-hydroxyvitamin D" OR cholecalciferol OR "vit D") OR ("Chromogranin A" OR CgA) OR ("tumor necrosis factor alpha" OR "TNF alpha" OR "TNF-α" OR TNF) OR ("Cortisol" OR hydrocortisone OR glucocorticoid)) AND ("serum" OR "plasma" OR "blood" OR "circulating" OR "biomarker*" OR "level*" OR concentration) AND ("case-control" OR "cross-sectional" OR "cohort" OR observational) NOT (review OR animal OR mice OR rats OR editorial OR letter OR "conference abstract").

After completing the electronic search, the search results were exported and managed using EndNote software. At this stage, duplicate entries were automatically identified and removed, preparing the dataset for further screening.

2.4. Eligibility Criteria

Studies were included if they met all criteria: (1) observational design (cross-sectional, case-control, or cohort); (2) publication in a peer-reviewed journal; (3) involvement of people diagnosed with ADHD by DSM-IV, DSM-5, or ICD criteria; (4) inclusion of a healthy control group; and (5) report of serum or plasma concentrations for at least one of the following: Vitamin D, CgA, TNF-α, or cortisol.

Studies were excluded if they were animal-based, interventional, or lacked baseline biomarker data, were reviews, or were editorials. Studies lacking a control group, duplicate datasets, or with insufficient data were also excluded.

2.5. Study Selection and Screening

The study selection process began with the initial identification of articles through database searches. After the automatic removal of duplicates, the remaining articles underwent a title and abstract screening. Full-text articles of eligible studies were then reviewed in detail using the inclusion and exclusion criteria. This selection process was conducted independently by two reviewers. Any disagreements between reviewers were resolved through discussion or, when necessary, by involving a third reviewer. Following this review, a total of 28 studies were identified as meeting all inclusion criteria and were included in the final meta-analysis. The entire process of study identification, screening, and inclusion was documented and summarized using a PRISMA flow diagram (Figure 1).

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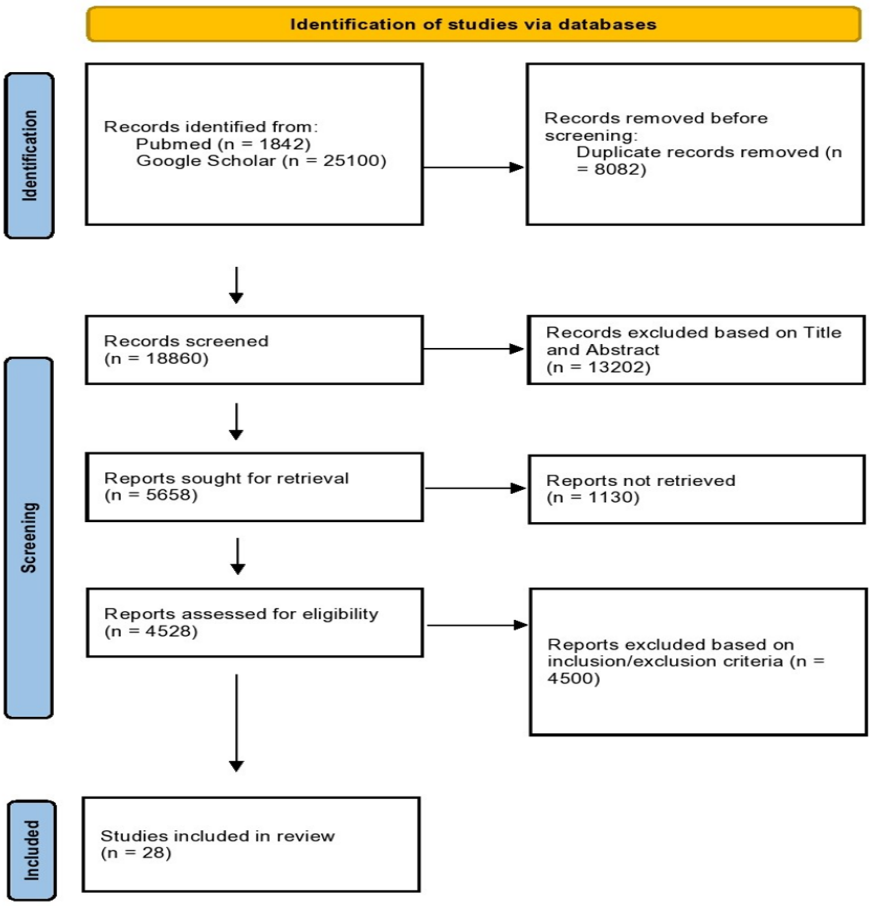

Figure 1. PRISMA chart showing selection and inclusion of studies (Page et al., 2021).

2.6. Data Extraction

Data were independently extracted by two reviewers using a standardized form. Extracted data included study characteristics (DOI, title, first author, year, country, journal, and study design), population details (sample size of ADHD and control groups), and biomarker information (type of biomarker assessed, e.g., cortisol; sample type, such as saliva; and assay or measurement methods used). For each study, we recorded biomarker levels in ADHD and control groups (means, standard deviations, or other reported values), effect sizes, and any reported correlations with symptom severity. Outcomes and conclusions as reported by the authors were also documented. Any discrepancies in data extraction were resolved through discussion or by involving a third reviewer. All extracted data were compiled for synthesis and statistical analysis using meta-analytic methods.

2.7. Statistical Analysis

Our meta-analysis followed the PRISMA guidelines. The effect sizes were calculated as Hedges' g (bias-corrected standardized mean differences), with 95% confidence intervals obtained using the inverse variance method. The random-effects model (restricted maximum-likelihood estimator) was applied to account for the study variability. The heterogeneity was quantified using tau^2, tau, I^2, and H statistics, with significance tested via Cochran's Q. Publication bias was assessed using funnel plots and, where appropriate, Egger's test. The sensitivity analyses omitted individual studies to identify influential outliers. Meta-regression examined potential moderators, including age, gender, and comorbidity. All analyses were performed using R packages "metafor" and "meta," with $p < 0.05$ considered significant.

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3. Results

Our meta-analysis assessed the differences in biomarker levels between patients with ADHD and controls, supporting the potential diagnostic roles of these biomarkers. Notably, for vitamin D, the random effects model demonstrated a large pooled effect size (SMD = -1.19, 95% CI = -2.04 to -0.33), which is statistically significant (p = 0.0068). This indicated that there are markedly lower serum levels in ADHD patients as compared to controls (Figure 2).

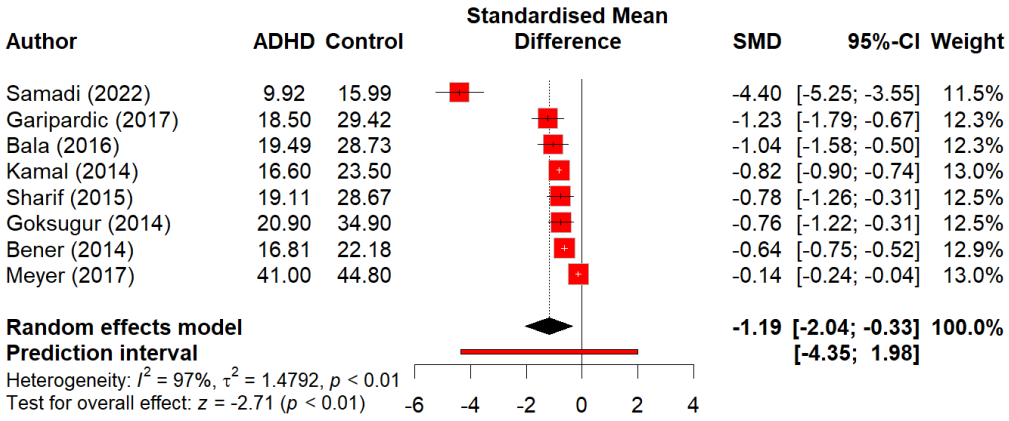

Figure 2. Standardized Mean Difference of Vitamin D between ADHD and Control.

However, the heterogeneity was extremely high (I^2 = 96.5%), suggesting substantial variability among studies. Furthermore, the sensitivity analysis revealed that no single study omission eliminated the heterogeneity, although the omission of Samadi (2022) [18] significantly reduced the effect size (SMD = -0.72) (Figure 3).

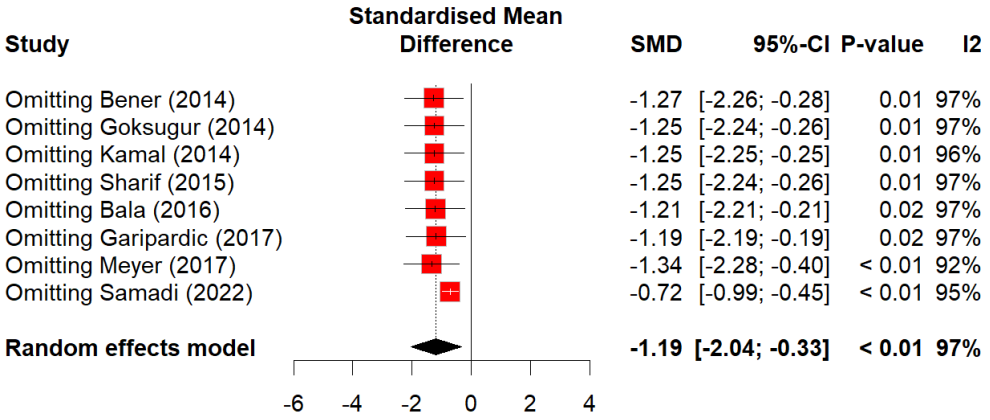

Figure 3. Sensitivity Analysis to find the source of heterogeneity in the Vitamin D effect Size.

In terms of the TNF-α, there was a smaller but significant reduction in ADHD patients (SMD = -0.39, 95% CI = -0.65 to -0.13, p = 0.0033) with low-to-moderate heterogeneity (I^2 = 22.0%) (Figure 4).

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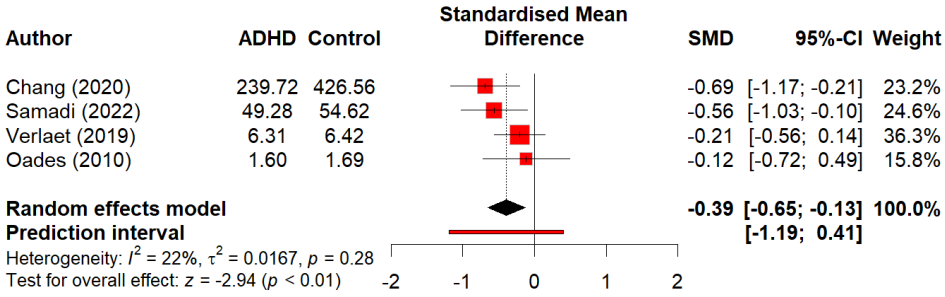

Figure 4. Standardized Mean Difference of Vitamin D between ADHD and Control.

The sensitivity analysis indicated that excluding Verlaet (2019) [19] or Chang (2020) [16] reduced heterogeneity to nearly zero, highlighting the possibility of study-specific effects (Figure 5).

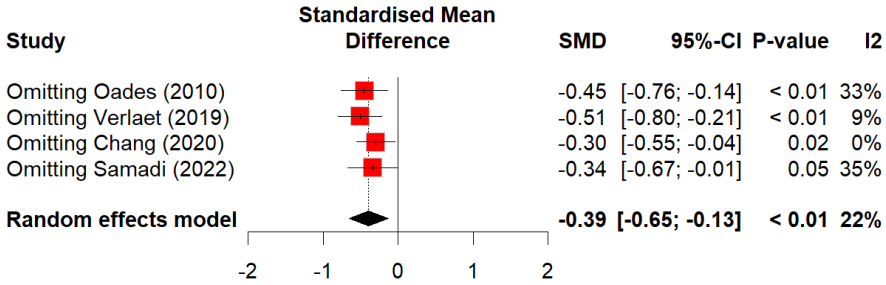

Figure 5. Sensitivity Analysis to find the source of heterogeneity in the TNF effect Size.

For the cortisol analysis, this analysis showed significantly lower levels in ADHD patients (SMD = -0.78, 95% CI = -1.48 to -0.08, p = 0.0280) (Figure 6).

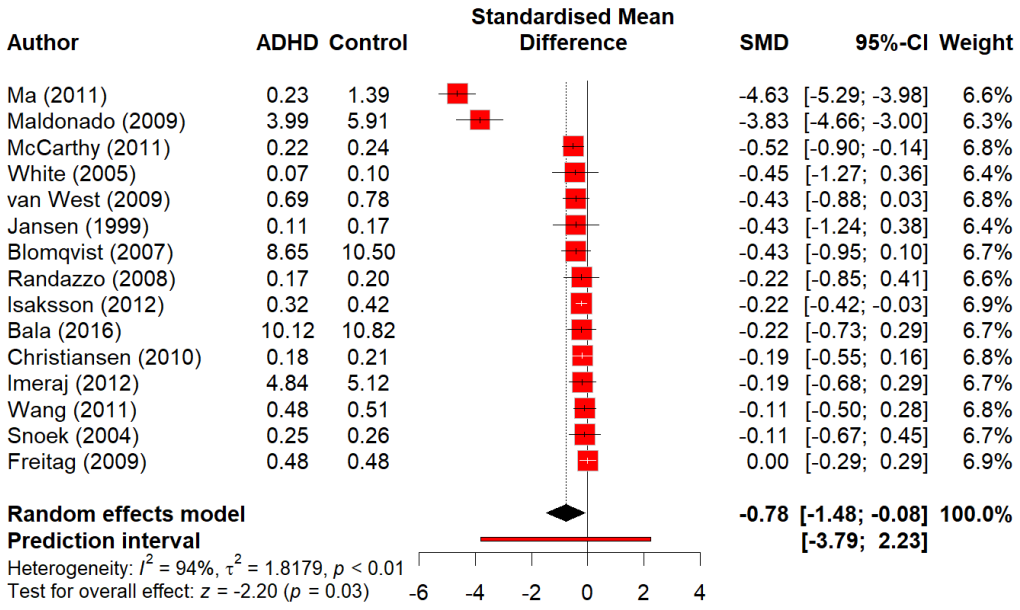

Figure 6. Standardized Mean Difference of Cortisol between ADHD and Control.

The heterogeneity was high (I^2 = 94.3%), and sensitivity analysis revealed that Ma (2011) [20] had a notable influence, with their omission reducing heterogeneity and altering effect size magnitude (Figure 7).

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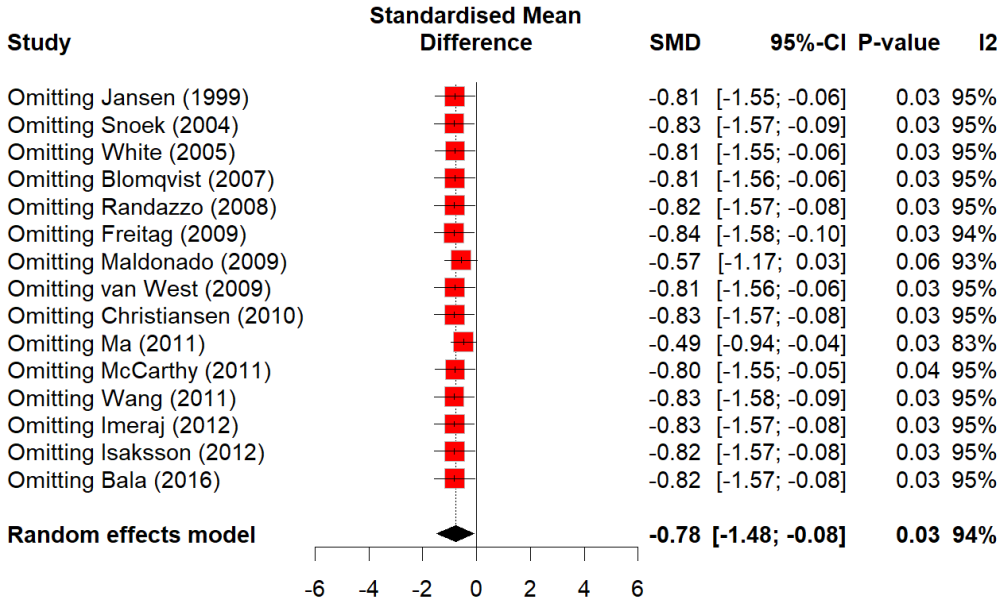

Figure 7. Sensitivity Analysis to find the source of heterogeneity in the Cortisol effect Size.

Table 1 presents the results of the meta-regression, which explored the predictors of vitamin D, TNF-α, and cortisol effect sizes in individuals with ADHD versus controls. For the predictors of vitamin D, age was positively associated with larger differences (Estimate = 0.33, p = 0.0044). Moreover, there was a higher proportion of males, which also predicted the greater effect sizes (Estimate = 1.59, p = 0.0071). Conversely, the comorbidities significantly reduced the effect size (Estimate = -1.23, p = 0.0227), indicating attenuation of the vitamin D–ADHD relationship in these populations. For TNF-α, no predictors were statistically significant. However, the male gender showed a near-significant positive trend (Estimate = 1.07, p = 0.0522), and age also showed a non-significant negative trend (Estimate = -1.28, p = 0.0822). For the effect size of cortisol, the age, gender, and the comorbidity were non-significant predictors (all p > 0.14).

Table 1. Meta regression to find out the predictors of the effect size of Vit. D, TNF-α, and Cortisol.

	Estimate	SE	z-value	p-value	95% CI
Vitamin D					
Age	0.3282	0.1151	2.8515	***0.0044***	0.1026 – 0.5537
Gender (Male)	1.5901	0.5902	2.6940	***0.0071***	0.4332 – 2.7469
Comorbidity (Yes)	-1.2340	0.5418	-2.2778	***0.0227***	-2.2958 – -0.1722
TNF-α					
Age	-1.2842	0.7389	-1.7379	0.0822	-2.7325 – 0.1641
Gender (Male)	1.0722	0.5524	1.9412	0.0522	-0.0104 – 2.1548
Cortisol					
Age	0.1825	0.2263	0.8065	0.4199	-0.2610 – 0.6261
Gender (Male)	1.4314	0.9826	1.4568	0.1452	-0.4944 – 3.3573
Comorbidity (Yes)	0.8745	0.7206	1.2136	0.2249	-0.5378 – 2.2868

The funnel plot (Figure 8), which assessed vitamin D levels in ADHD, revealed a clear asymmetry, with most studies clustered near the zero-effect size on the right side, and a few extreme negative values on the left side. Ideally, the studies should be arranged symmetrically in the plot; however, this imbalance, particularly the absence of small studies with positive or null effects, suggests the possibility of publication bias or selective reporting. The larger studies consistently showed the moderate-to-large negative effects, while smaller ones vary widely. This pattern revealed

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a high risk of bias in vitamin D analysis, suggesting that both methodological variation and small-study effects may influence the observed association.

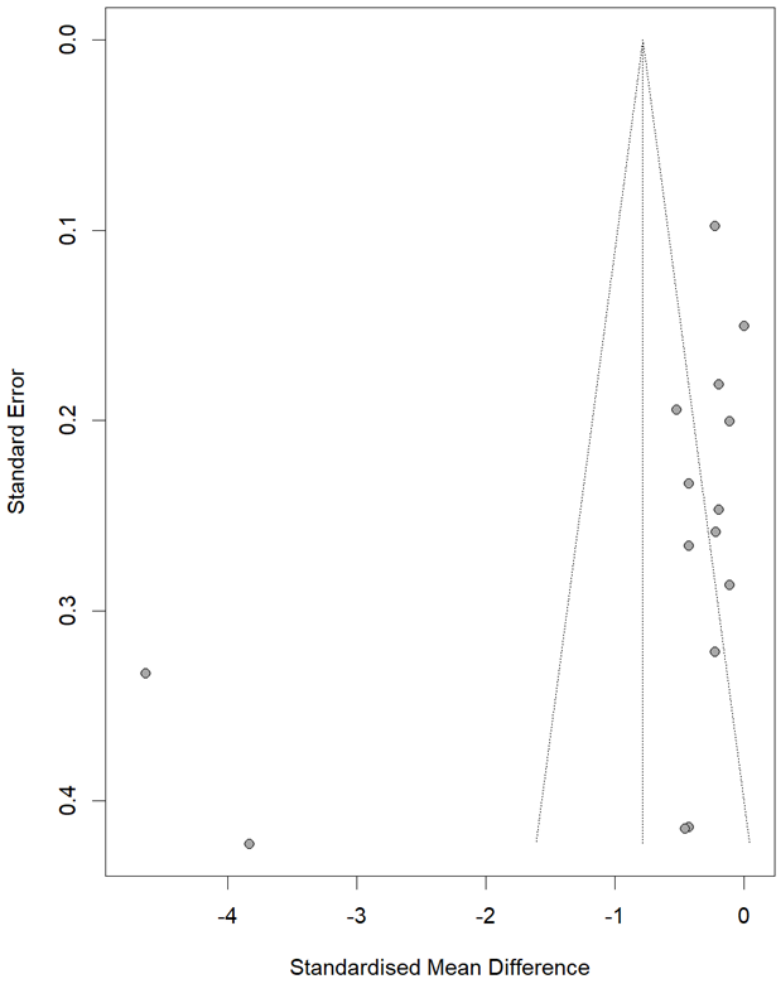

Figure 8. Assessment of risk of bias with funnel plot.

4. Discussion

This meta-analysis pooled data from 28 observational studies to examine the diagnostic validity of four serum biomarkers in patients with ADHD: Vitamin D, TNF-α, cortisol, and CgA. Our results showed that significantly lower levels of vitamin D, TNF-α, and cortisol were present across the ADHD groups compared with healthy controls, with no consistent effect for CgA. These findings shed new light on the possible utility of neuroendocrine and inflammatory markers in the diagnosis and conceptualization of ADHD, a heterogeneous and multifaceted neurodevelopmental disorder.

4.1. Vitamin D

The most significant changed biomarker was Vitamin D, with a large and statistically significant pooled effect size (SMD = -1.19, $p < 0.01$), showing that individuals with ADHD always have reduced circulating levels of Vitamin D. This is consistent with previous research that has found a significant negative correlation of serum Vitamin D with ADHD diagnosis. For example, studies by M. Sharif et al. (2015) [17], Fasihpour et al. (2020) [21], and Elshahawi et al. (2024) [22] have established that

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Vitamin D deficiency is considerably more likely to occur in children with ADHD and that deficiency is associated with symptom severity.

The neurobiological basis of the association is supported by Vitamin D's role in regulating dopamine production, neural differentiation, neurotrophic factor expression, and immune homeostasis [23]. The association is moderated by demographic and clinical factors, as per our meta-regression findings, with greater effects observed in samples with older and male prevalence, and lesser effects in research that includes comorbid conditions. High heterogeneity and asymmetry of the funnel plots, however, reflect possible publication bias and study-level heterogeneity, which call for interpretive caution.

4.2. Cortisol

Our meta-analysis also revealed significantly lower cortisol in ADHD patients (SMD = -0.78, $p = 0.03$), indicating a potential role of hypothalamic-pituitary-adrenal axis (HPA) dysregulation. This dysregulation commonly manifests as blunted cortisol rhythms or lower basal levels that have been repeatedly observed in ADHD populations and may contribute to under-arousal and poor behavioral inhibition [16,24]. Longitudinal profiling has shown that ADHD children often display flatter diurnal cortisol slopes, which reflects disrupted circadian regulation of arousal [25]. This emerging evidence highlights the involvement of HPA axis dysregulation in ADHD. Various independent studies corroborate this report. For example, Northover et al. [26] and El Ghamry et al. [27] each reported significantly lower basal or morning cortisol in ADHD patients, with Chang et al. [16] providing meta-analytic corroboration of this blunted cortisol profile. Low cortisol could potentially play a role in under-arousal and inefficient stress regulation: features which are classically observed in ADHD behavior and cognition.

Interestingly, pharmacological therapy with stimulants like methylphenidate has also been shown to normalize cortisol in the long term, which has the potential to be a dynamic treatment marker [28]. Our results, however, showed considerable heterogeneity and wide prediction intervals, which reflect heterogeneity in individual cortisol reactivity, as well as the effects of stress, comorbid anxiety, and methodological variation (e.g., saliva vs. plasma measurements).

4.3. TNF-α

TNF-α, the principal pro-inflammatory cytokine, was also decreased in ADHD patients (SMD = -0.39, $p < 0.01$). This is contrary to the broad expectation of raised inflammatory markers in psychiatric illness but is in line with findings from Chang et al. [16] and other observational research [29]. It may be secondary to frequent suppression of cortisol chronically, because glucocorticoids regulate immune function, or may be compensatory mechanisms in neuroimmune communication [30].

Although the role of inflammation in ADHD is debated, early immune insults to neurodevelopment can create lasting immune signaling alterations rather than necessarily leading to chronic inflammation. The limited heterogeneity in the TNF-α analysis provides further support to this finding, but further mechanistic and longitudinal work will be necessary to determine its clinical relevance.

4.4. Chromogranin A

While CgA was indicated as an interesting marker due to its role in stimulation of the sympathetic nervous system and in neuroendocrine signaling [31], our meta-analysis did not have sufficient studies with quantitative data to allow for effect estimation by pooling. No disparity in the data available in the limited number of studies between the ADHD and control groups was seen. Unlike cortisol or TNF-α, CgA has been studied to a lesser extent in cardiovascular or tumor-related diseases, and its role in neuropsychiatric disorders is not well explored.

This lack of a distinct cut signal could be due to either the biological irrelevance of CgA in the pathogenesis of ADHD or technical challenges in existing studies. Since CgA is co-secreted with

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catecholamines, CgA could be explored under acute stress or stimulant challenge conditions, rather than at baseline, in the future.

4.5. Implications and Limitations

Collectively, based on our findings, it is clear that Vitamin D, cortisol, and TNF-α are dysregulated in individuals with ADHD and could potentially be employed as peripheral biomarkers for diagnosis or treatment monitoring. However, some limitations must be considered:

- Extreme heterogeneity in Vitamin D and cortisol levels may limit generalizability.
- Publication bias existed in the Vitamin D literature.
- The limited number of studies of CgA and variable assay methods between biomarkers weaken these conclusions.
- Confounders like comorbidities, drug use, age, and time of sampling were controlled variably.

Longitudinal follow-up of biomarkers ought to be the priority for future research, including multi-omics, and standardizing protocols for sample collection. Examination of biomarker changes before and after treatment can also reveal their utility as markers of treatment response or disease status.

5. Conclusions

This meta-analysis confirms the correlation of ADHD with significantly lower serum Vitamin D, TNF-α, and cortisol levels with neuroimmune and neuroendocrine impairment.

These biomarkers, especially Vitamin D, have the potential for diagnostic utility.

Hence, biomarker integration can enhance the diagnosis and treatment of ADHD.

Author Contributions: Conceptualization, I.A.H., R.M.H. and R.P.D.; methodology, R.M.H. and L.L.H.; software, B.V.S. and I.D.; validation, I.A.H., I.H. and R.P.D.; formal analysis, I.L.S., D.M.T. and C.C.T.; investigation, R.M.H., R.J. and L.L.H.; resources, I.A.H. and R.J.; data curation, I.D.; writing—original draft preparation, I.A.H. and R.M.H.; writing—review and editing, I.A.H. and R.P.D.; visualization, L.L.H., R.J. and I.H.; supervision, R.P.D.; project administration, L.L.H., I.L.S., D.M.T. and I.D.; funding acquisition, L.L.H. and R.J. All authors have read and agreed to the published version of the manuscript.

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Abbreviations

The following abbreviations are used in this manuscript:

ADHD	Attention-Deficit/Hyperactivity Disorder
TNF	Tumor Necrosis Factor
CI	Confidence Interval
SE	Standard Error
CgA	Chromogranin A
GBD	Global Burden of Disease
SMD	Standardised Mean Difference

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HPA Hypothalamic-pituitary-adrenal axis

References

1. Musullulu, H. Evaluating Attention Deficit and Hyperactivity Disorder (ADHD): A Review of Current Methods and Issues. *Front Psychol* **2025**, *16*, 1466088, doi:10.3389/fpsyg.2025.1466088.
2. Sanwo, O.; Huzair, H. What's New in Attention-Deficit/Hyperactivity Disorder: Updates on Assessment and Management. *Paediatrics and Child Health* **2022**, *32*, 282–289, doi: 10.1016/j.paed.2022.05.002.
3. Cortese, S.; Song, M.; Farhat, L.C.; Yon, D.K.; Lee, S.W.; Kim, M.S.; Park, S.; Oh, J.W.; Lee, S.; Cheon, K.-A.; et al. Incidence, Prevalence, and Global Burden of ADHD from 1990 to 2019 across 204 Countries: Data, with Critical Re-Analysis, from the Global Burden of Disease Study. *Mol Psychiatry* **2023**, *28*, 4823–4830, doi:10.1038/s41380-023-02228-3.
4. Thomas, R.; Sanders, S.; Doust, J.; Beller, E.; Glasziou, P. Prevalence of Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis. *Pediatrics* **2015**, *135*, e994-1001, doi:10.1542/peds.2014-3482.
5. Synergy for the Influence of the Month of Birth in ADHD (SIMBA) study group Association between Relative Age at School and Persistence of ADHD in Prospective Studies: An Individual Participant Data Meta-Analysis. *Lancet Psychiatry* **2023**, *10*, 922–933, doi:10.1016/S2215-0366(23)00272-9.
6. Martin, A.F.; Rubin, G.J.; Rogers, M.B.; Wessely, S.; Greenberg, N.; Hall, C.E.; Pitt, A.; Logan, P.E.; Lucas, R.; Brooks, S.K. The Changing Prevalence of ADHD? A Systematic Review. *J Affect Disord* **2025**, *388*, 119427, doi:10.1016/j.jad.2025.119427.
7. Sharma, P.; Gupta, R.K.; Banal, R.; Majeed, M.; Kumari, R.; Langer, B.; Akhter, N.; Gupta, C.; Raina, S.K. Prevalence and Correlates of Attention Deficit Hyperactive Disorder (ADHD) Risk Factors among School Children in a Rural Area of North India. *J Family Med Prim Care* **2020**, *9*, 115–118, doi:10.4103/jfmpc.jfmpc_587_19.
8. Umar, M.U.; Obindo, J.T.; Omigbodun, O.O. Prevalence and Correlates of ADHD Among Adolescent Students in Nigeria. *J Atten Disord* **2018**, *22*, 116–126, doi:10.1177/1087054715594456.
9. Ayano, G.; Demelash, S.; Gizachew, Y.; Tsegay, L.; Alati, R. The Global Prevalence of Attention Deficit Hyperactivity Disorder in Children and Adolescents: An Umbrella Review of Meta-Analyses. *J Affect Disord* **2023**, *339*, 860–866, doi:10.1016/j.jad.2023.07.071.
10. Ginsberg, Y.; Quintero, J.; Anand, E.; Casillas, M.; Upadhyaya, H.P. Underdiagnosis of Attention-Deficit/Hyperactivity Disorder in Adult Patients: A Review of the Literature. *Prim Care Companion CNS Disord* **2014**, *16*, PCC.13r01600, doi:10.4088/PCC.13r01600.
11. Gore, M.; Morgan, J. Children with Attention Deficit Hyperactivity Disorder in India: Strengthening Diagnosis, Support, Training and Research. *Journal of Indian Association for Child and Adolescent Mental Health* **2025**, *21*, 17–22, doi:10.1177/09731342241310558.
12. Quinn, P.O.; Madhoo, M. A Review of Attention-Deficit/Hyperactivity Disorder in Women and Girls: Uncovering This Hidden Diagnosis. *Prim Care Companion CNS Disord* **2014**, *16*, PCC.13r01596, doi:10.4088/PCC.13r01596.
13. Song, P.; Zha, M.; Yang, Q.; Zhang, Y.; Li, X.; Rudan, I.; Global Health Epidemiology Reference Group (GHERG) The Prevalence of Adult Attention-Deficit Hyperactivity Disorder: A Global Systematic Review and Meta-Analysis. *J Glob Health* **2021**, *11*, 04009, doi:10.7189/jogh.11.04009.
14. Anand, D.; Colpo, G.D.; Zeni, G.; Zeni, C.P.; Teixeira, A.L. Attention-Deficit/Hyperactivity Disorder And Inflammation: What Does Current Knowledge Tell Us? A Systematic Review. *Front Psychiatry* **2017**, *8*, 228, doi:10.3389/fpsyt.2017.00228.
15. Scassellati, C.; Bonvicini, C.; Faraone, S.V.; Gennarelli, M. Biomarkers and Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analyses. *J Am Acad Child Adolesc Psychiatry* **2012**, *51*, 1003-1019.e20, doi:10.1016/j.jaac.2012.08.015.
16. Chang, J.P.-C.; Su, K.-P.; Mondelli, V.; Pariante, C.M. Cortisol and Inflammatory Biomarker Levels in Youths with Attention Deficit Hyperactivity Disorder (ADHD): Evidence from a Systematic Review with Meta-Analysis. *Transl Psychiatry* **2021**, *11*, 430, doi:10.1038/s41398-021-01550-0.

 doi:10.20944/preprints202602.1694.v1

17. Sharif, M.R.; Madani, M.; Tabatabaei, F.; Tabatabaee, Z. The Relationship between Serum Vitamin D Level and Attention Deficit Hyperactivity Disorder. *Iran J Child Neurol* **2015**, *9*, 48–53.
18. Samadi, M.; Gholami, F.; Seyedi, M.; Jalali, M.; Effatpanah, M.; Yekaninejad, M.; Abdolahi, M.; Chamari, M.; Honarvar, N. Effect of Vitamin D Supplementation on Inflammatory Biomarkers in School-Aged Children with Attention Deficit Hyperactivity Disorder. *International Journal of Clinical Practice* **2022**, *2022*, 1–7, doi:10.1155/2022/1256408.
19. Verlaet, A.A.J.; Breynaert, A.; Ceulemans, B.; De Bruyne, T.; Fransen, E.; Pieters, L.; Savelkoul, H.F.J.; Hermans, N. Oxidative Stress and Immune Aberrancies in Attention-Deficit/Hyperactivity Disorder (ADHD): A Case-Control Comparison. *Eur Child Adolesc Psychiatry* **2019**, *28*, 719–729, doi:10.1007/s00787-018-1239-4.
20. Ma, L.; Chen, Y.-H.; Chen, H.; Liu, Y.-Y.; Wang, Y.-X. The Function of Hypothalamus-Pituitary-Adrenal Axis in Children with ADHD. *Brain Res* **2011**, *1368*, 159–162, doi:10.1016/j.brainres.2010.10.045.
21. Fasihpour, B.; Moayeri, H.; Shariat, M.; Keihanidoust, Z.; Effatpanah, M.; Khedmat, L. Vitamin D Deficiency in School-Age Iranian Children with Attention-Deficit/Hyperactivity Disorder (ADHD) Symptoms: A Critical Comparison with Healthy Controls. *Child Neuropsychol* **2020**, *26*, 460–474, doi:10.1080/09297049.2019.1665638.
22. Elshahawi, H.; Amin, G.; Khalil, S.; Kasem, R.; Mostafa, A. Serum Vitamin D Level in Children with Attention Deficit Hyperactivity Disorder (ADHD). *QJM: An International Journal of Medicine* **2024**, *117*, doi:10.1093/qjmed/hcae175.491.
23. Sahin, N.; Altun, H.; Kurutas, E.B.; Balkan, D. Vitamin D and Vitamin D Receptor Levels in Children with Attention-Deficit/Hyperactivity Disorder. *Neuropsychiatr Dis Treat* **2018**, *14*, 581–585, doi:10.2147/NDT.S158228.
24. Isaksson, J.; Nilsson, K.W.; Nyberg, F.; Hogmark, A.; Lindblad, F. Cortisol Levels in Children with Attention-Deficit/Hyperactivity Disorder. *J Psychiatr Res* **2012**, *46*, 1398–1405, doi:10.1016/j.jpsychires.2012.08.021.
25. Imeraj, L.; Antrop, I.; Roeyers, H.; Swanson, J.; Deschepper, E.; Bal, S.; Deboutte, D. Time-of-Day Effects in Arousal: Disrupted Diurnal Cortisol Profiles in Children with ADHD. *J Child Psychol Psychiatry* **2012**, *53*, 782–789, doi:10.1111/j.1469-7610.2012.02526.x.
26. Northover, C.; Thapar, A.; Langley, K.; Fairchild, G.; van Goozen, S.H.M. Cortisol Levels at Baseline and under Stress in Adolescent Males with Attention-Deficit Hyperactivity Disorder, with or without Comorbid Conduct Disorder. *Psychiatry Res* **2016**, *242*, 130–136, doi:10.1016/j.psychres.2016.05.052.
27. El Ghamry, R.H.; Mohamed, M.M.; Azzam, H.M.; Elhabiby, M.M.; Hasan, H.M.; Hashish, A.F.; Elhamshary, M.M.; Barakat, D.M.H. Aggression in ADHD: Relation to Salivary Cortisol. *Middle East Current Psychiatry* **2021**, *28*, 25, doi:10.1186/s43045-021-00104-w.
28. Connolly, J.J.; Glessner, J.T.; Elia, J.; Hakonarson, H. ADHD & Pharmacotherapy: Past, Present and Future: A Review of the Changing Landscape of Drug Therapy for Attention Deficit Hyperactivity Disorder. *Ther Innov Regul Sci* **2015**, *49*, 632–642, doi:10.1177/2168479015599811.
29. Corominas-Roso, M.; Armario, A.; Palomar, G.; Corrales, M.; Carrasco, J.; Richarte, V.; Ferrer, R.; Casas, M.; Ramos-Quiroga, J.A. IL-6 and TNF-α in Unmedicated Adults with ADHD: Relationship to Cortisol Awakening Response. *Psychoneuroendocrinology* **2017**, *79*, 67–73, doi:10.1016/j.psyneuen.2017.02.017.
30. Kozłowska, A.; Wojtacha, P.; Równiak, M.; Kolenkiewicz, M.; Huang, A.C.W. ADHD Pathogenesis in the Immune, Endocrine and Nervous Systems of Juvenile and Maturating SHR and WKY Rats. *Psychopharmacology (Berl)* **2019**, *236*, 2937–2958, doi:10.1007/s00213-019-5180-0.
31. Deftos, L.J. Chromogranin A: Its Role in Endocrine Function and as an Endocrine and Neuroendocrine Tumor Marker*. *Endocr Rev* **1991**, *12*, 181–188, doi:10.1210/edrv-12-2-181.