Scientific Research Publishing

Open Journal of Pediatrics, 2026, 16(5), 706-719
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

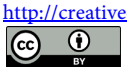
Potential Therapeutic Benefit of Combined *Bacopa monnieri* (Brahmi) and Piracetam in Children with Attention-Deficit/Hyperactivity Disorder: A Pilot Prospective Observational Study

Mishra Udbhatt

Department of Pediatrics, Ambalike Clinic, Padmshri Dr. Mohan Mishra Path, Bengali Tola, Laheriasarai, Darbhanga, Bihar, India
Email: drudbhatt@gmail.com

How to cite this paper: Udbhatt, M. (2026) Potential Therapeutic Benefit of Combined *Bacopa monnieri* (Brahmi) and Piracetam in Children with Attention-Deficit/Hyperactivity Disorder: A Pilot Prospective Observational Study. *Open Journal of Pediatrics*, **16**, 706-719.
https://doi.org/10.4236/ojped.2026.165069

Received: August 10, 2026
Accepted: September 21, 2026
Published: September 24, 2026



Abstract

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is a prevalent neurodevelopmental disorder in pediatric populations. Concerns regarding adverse effect profiles, long-term tolerability, and compliance with central nervous system stimulants have stimulated clinical interest in complementary, adjunctive, and nootropic therapeutic strategies. **Objective:** To generate preliminary naturalistic data on the clinical safety, tolerability, feasibility, non-responder characteristics, and behavioral trajectories in pediatric ADHD following a six-month regimen of combined *Bacopa monnieri* and piracetam. **Methods:** A pilot, prospective, naturalistic observational study screened a consecutive series of 33 pediatric patients aged 5 - 10 years presenting to an outpatient pediatric clinic in Darbhanga, Bihar, India. All participants were regular mainstream school-attending children presenting with study inattention and academic underperformance. Independent clinical diagnostic interviews and outcome tracking were conducted directly by the primary investigator (Dr. Udbhatt Mishra, Pediatric Specialist) using DSM-5 diagnostic criteria and validated via the Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS). Safety and tolerability were monitored through monthly structured clinical symptom checklists, vital sign tracking, and physical examinations. To mitigate reporting bias in the absence of teacher ratings, monthly Vanderbilt evaluations were clinician-administered with qualitative cross-examination and direct behavioral observation. Cross-situational impairment was confirmed across all subjects. Of 33 eligible patients, 4 declined the pharmacological pro-

tocol, and 29 were enrolled. Over the 6-month follow-up, 9 patients were lost to follow-up, yielding 20 patients for per-protocol analysis (ADHD Combined: 60%, n = 12; Predominantly Inattentive: 30%, n = 6; Predominantly Hyperactive/Impulsive: 10%, n = 2). Baseline characteristics between completers and dropouts were compared to evaluate selection bias, and sensitivity intention-to-treat (ITT) analyses (BOCF and LOCF) across all 29 enrolled subjects were conducted. Core ADHD symptoms (18 items) were evaluated using a psychometrically validated Average Item Score (total score /18, scale: 0.00 - 3.00), and clinical response was defined using the ≥30% symptom reduction threshold. Patients received daily oral therapy comprising standardized *Bacopa monnieri* extract tablets (250 mg once daily; Himalaya Wellness Company, HPLC/HPTLC standardized) and piracetam tablets (250 mg twice daily; 500 mg/day). Statistical evaluations included paired t-tests, Wilcoxon signed-rank tests, 95% confidence intervals (CI), and Cohen's d effect sizes. **Results:** High treatment adherence was documented across the completed cohort (mean pill count adherence: 94.2% ± 4.1%; 100% ≥ 85%). Comparison of baseline parameters between completers (n = 20) and participants lost to follow-up (n = 9) revealed no statistically significant differences in age (7.4 ± 1.6 vs. 7.2 ± 1.5 years; p = 0.75), baseline Vanderbilt Average Item Score (2.75 ± 0.24 vs. 2.71 ± 0.26; p = 0.69), ADHD subtype distribution (p = 0.88), or functional impairment rates, confirming negligible baseline attrition selection bias. In the per-protocol cohort (n = 20), mean Vanderbilt Average Item Score significantly decreased from 2.75 ± 0.24 at baseline to 1.50 ± 0.51 post-treatment (t = 3.05, p = 0.007; Wilcoxon: p = 0.008; Cohen's d = 0.68). In sensitivity ITT analysis across all enrolled participants (N = 29) using conservative Baseline Observation Carried Forward (BOCF/non-responder assumption), the mean symptom reduction remained statistically significant (baseline 2.74 ± 0.24 to endpoint 1.88 ± 0.70, mean reduction: 0.86 points; paired t = 6.42, p < 0.001; Cohen's d = 1.19), with an overall ITT response rate (≥30% reduction) of 34.5% (10/29). In per-protocol mapping, marked improvement was observed in 50% (n = 10), stable response in 25% (n = 5), and symptom worsening in 25% (n = 5); worsening participants recovered uneventfully without behavioral crises or clinical toxicities. Transient mild nausea (n = 2, 10%) and delayed sleep onset (n = 1, 5%) resolved spontaneously; no serious adverse events occurred. **Conclusion:** Combined administration of *Bacopa monnieri* and piracetam demonstrated favorable clinical feasibility, good clinical tolerability, and high caregiver adherence in this naturalistic pilot cohort, alongside an observed downward shift in parent-reported symptom scores supported by both per-protocol and conservative ITT analyses. Because this single-arm, observational study was conducted in a resource-limited setting without extramural funding and lacked standardized serial biochemical laboratory safety monitoring (specifically hepatic and renal function tests), was restricted to male participants, lacked teacher-informant ratings, and lacked a control group, these findings provide preliminary exploratory evidence that cannot establish efficacy or complete organ-specific safety. Future prospective, multi-inform-

ant, double-blind randomized clinical trials must incorporate mandatory standardized laboratory safety panels including comprehensive liver and kidney function testing.

Keywords

ADHD, *Bacopa monnieri*, Brahmi, Piracetam, Nootropics, Pediatrics, DSM-5, Intention-to-Treat, Safety Monitoring, Hepatorenal Function

1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) affects approximately 5% - 7% of children worldwide and is characterized by pervasive patterns of inattention, hyperactivity, and impulsivity leading to academic, social, and behavioral impairments [1] [2]. Although central nervous system stimulants (e.g., methylphenidate) and non-stimulant agents (e.g., atomoxetine) remain standard first-line therapies [3], interest in complementary and alternative medicine (CAM) approaches continues to grow [4]. This interest is driven by caregiver concerns regarding appetite suppression, insomnia, emotional blunting, potential dependency, and variable access in low- and middle-income countries (LMICs) [5] [6].

In resource-constrained settings across India, specialized child psychiatry and tertiary behavioral therapy infrastructure remains sparse outside metropolitan zones [7]. In these regional environments, alternative pharmacological strategies with favorable safety profiles are frequently explored. Piracetam, a cyclic GABA derivative, has been shown in preclinical models to modulate neuronal membrane fluidity, microcirculation, and cerebral metabolic activity [8]. It is widely accepted by families in regional clinical practices as a familiar, well-tolerated cognitive-supportive agent. In parallel, *Bacopa monnieri* (Brahmi), a revered Ayurvedic botanical, enhances cholinergic signaling, upregulates synaptic plasticity, and provides neuroprotective antioxidant modulation in basic laboratory models [9] [10]. Pediatric studies indicate that *Bacopa monnieri* is associated with improvements in working memory, divided attention, and behavioral self-regulation [11]. Together, Bacopa and piracetam present a hypothesized neurochemical rationale targeting both cholinergic synaptic mechanisms and cellular metabolic support.

This pilot study was conducted to generate preliminary observational data regarding behavioral response trajectories, clinical subtype presentations, baseline functional impairments, treatment adherence, safety, and clinical feasibility associated with this combined regimen in a consecutive series of pediatric male patients presenting to a regional pediatric clinic in Bihar, India.

2. Materials and Methods

2.1. Study Design and Setting

This was an exploratory, pilot, prospective, naturalistic observational study con-

ducted at the Department of Pediatrics, Ambalike Clinic, Darbhanga, Bihar, India, tracking clinical and safety parameters over a six-month observation period.

2.2. Ethics and Regulatory Governance

The study protocol received ethical clearance from the Institutional Ethics Committee (IEC) of Ambalike Clinic (Ref No: AC-IEC/2025/06-02, Date: June 18, 2025; Table 1). The research adhered to the Declaration of Helsinki and Indian Council of Medical Research (ICMR) ethical guidelines. Written informed parental consent and age-appropriate pediatric assent were obtained prior to enrollment.

Table 1. Ethical approval details & governance matrix.

Parameter	Details/Guidelines
Reviewing Board	Institutional Ethics Committee (IEC) - Ambalike Clinic
Location/Address	Ambalike Clinic, Padmshri Dr. Mohan Mishra Path, Bengali Tola, Laheriasarai, Darbhanga, Bihar, 846001, India
Approval Reference	AC-IEC/2025/06-02 (Date of Approval: June 18, 2025)
IEC Leadership	Dr. Sonam Chungkula Bhutia (Chairperson); Mr. Prashant Kumar Jha (Member Secretary)
Mandatory Terms	Conformity with Declaration of Helsinki and ICMR guidelines; de-identified charting; mandatory 24-hour serious adverse event reporting.

2.3. DSM-5 Diagnostic Ascertainment & Educational Context

All clinical diagnostic evaluations were performed directly and independently by the primary investigator, Dr. Udbhatt Mishra (Pediatric Specialist). Diagnostic verification adhered to strict Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria [12] through semi-structured clinical interviews administered to parents/guardians alongside direct interactive child behavioral observations.

All enrolled participants were regular, mainstream school-attending children whose primary presenting complaint from parents was severe difficulty concentrating in studies, classroom inattention, and academic underachievement. None of the children attended specialized ADHD-oriented educational institutions or received individualized educational plans (IEPs). To establish cross-situational impairment in accordance with DSM-5 Criterion C and D, functional disruption was verified across at least two distinct environments (academic/classroom and home/interpersonal settings). Baseline functional impairment was systematically characterized across three primary functional domains: 1) Academic Performance (learning efficiency, classroom disruption, homework completion failures); 2) Peer Relationships (conflict during social play, impulsivity in peer groups); and 3) Home/Family Functioning (parental distress, task non-compliance, defiance during daily routines).

2.4. Concomitant Therapies & Interventions

Throughout the 6-month observation window, participants did not receive formal behavioral therapy, psychotherapy, sensory integration therapy, institutional remedial education, or special educational support services, as these resources were unavailable in the local practice ecosystem. Furthermore, no concurrent neurotropic supplements, micronutrient mega-doses, herbal concoctions, or standard psychostimulant/non-stimulant ADHD pharmacotherapies were permitted or administered, ensuring the observational data reflects isolated dual-regimen exposure.

2.5. Participant Selection, Patient Flow, and Attrition Analysis

The study cohort was drawn from a consecutive series of 33 pediatric patients presenting with behavioral concerns to the outpatient department (OPD) of Ambalike Clinic. The complete progression of participant screening, pre-treatment exclusions, allocation, 6-month longitudinal tracking, and attrition mapping is illustrated in the CONSORT-style participant flow diagram (Figure 1).

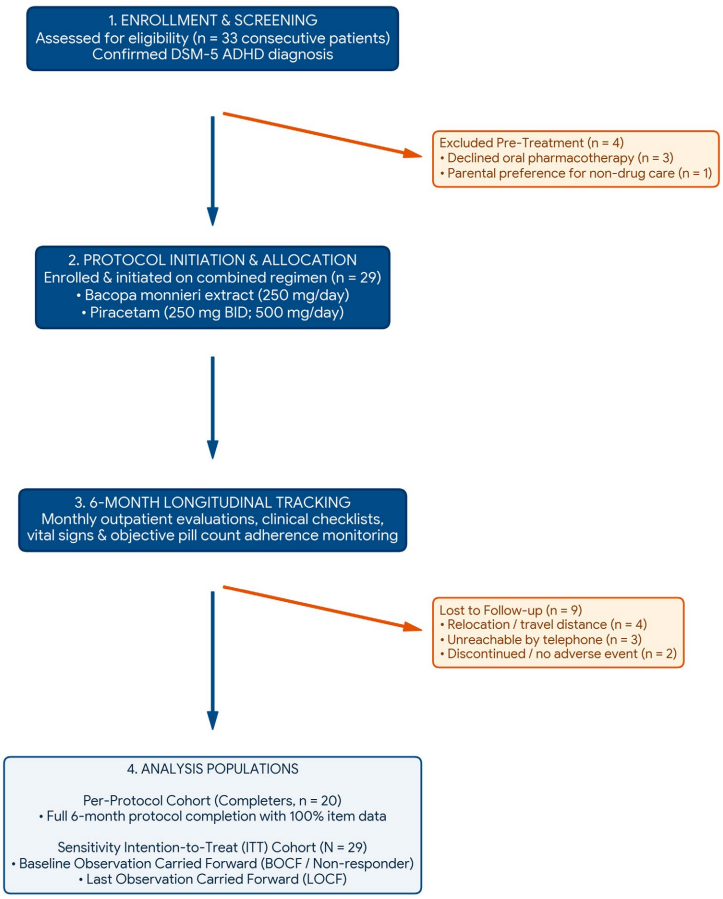


Figure 1. CONSORT-style participant flow diagram depicting patient screening (n = 33), pre-treatment exclusions (n = 4), protocol initiation on combined *Bacopa monnieri* and piracetam (n = 29), 6-month follow-up tracking (lost to follow-up, n = 9), and final per-protocol (n = 20) and intention-to-treat (n = 29) analysis cohorts.

- **Inclusion Criteria:** Male sex; aged 5 - 10 years at baseline; formal DSM-5 ADHD diagnosis verified by independent clinical interview and confirmed via the Vanderbilt ADHD Diagnostic Parent Rating Scale [13]; presence of documented cross-situational functional impairment; complete 6-month longitudinal tracking.
- **Exclusion Criteria:** Major co-existing neurological conditions (e.g., active epilepsy, cerebral palsy); severe psychiatric comorbidities (e.g., autism spectrum disorder, bipolar disorder); concurrent use of stimulant or non-stimulant ADHD medications; refusal of prescribed therapy; or loss to follow-up.

2.6. Treatment Protocol, Product Standardization & Dosing

Participants received a standardized daily oral combined regimen maintained over six continuous months: 1) standardized commercial *Bacopa monnieri* extract tablets (250 mg orally once daily in the morning; Himalaya Wellness Company, Makali, Bengaluru, Karnataka, India; HPLC/HPTLC standardized to active bacosides); and 2) commercial pediatric piracetam tablets (250 mg orally twice daily; total daily dose: 500 mg). A fixed age-bracketed dosing scheme (250 mg/day Bacopa; 500 mg/day piracetam) was utilized across the 5 - 10-year age band based on available solid oral unit formulations to prevent caregiver dosing errors and ensure strict compliance.

2.7. Psychometric Validation of Outcome Measures, Bias Mitigation & 30% Threshold

The primary outcome was change on the standardized Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS) [13]. The 18 core DSM-5 symptom items evaluate two psychometrically validated factor dimensions: Inattention (Items 1 - 9) and Hyperactivity/Impulsivity (Items 10 - 18), scored on a 4-point Likert scale (0 = Never, 1 = Occasionally, 2 = Often, 3 = Very Often). Functional impairment was evaluated across 8 performance items (Items 48 - 55) [13] [14]. A combined Average Item Score was calculated by dividing the sum of the 18 core DSM items by 18 (scale: 0.00 - 3.00) [15]-[17]. Caregivers completed all 18 core items during structured clinic interviews.

2.7.1. Bias Mitigation & Educational Context

To mitigate parental reporting bias in the absence of teacher ratings (which were logistically precluded by regional schooling constraints), monthly Vanderbilt scales were administered directly by the pediatric specialist, cross-examining parent ratings against concrete behavioral examples and direct interactive behavioral observations of the child.

2.7.2. Handling of Missing Data, Per-Protocol vs. ITT Rationale, and Response Threshold

The primary analysis was conducted on a complete-case per-protocol cohort (n = 20) with 100% verified item completion across 6 continuous months. To account

for attrition and ensure complete transparency, sensitivity Intention-to-Treat (ITT) analyses were conducted across all N = 29 enrolled patients using: 1) Baseline Observation Carried Forward (BOCF), treating dropouts as complete non-responders (0% symptom reduction); and 2) Last Observation Carried Forward (LOCF) using intermediate recorded scores. Clinical response was operationalized as a ≥30% reduction in the Vanderbilt score from baseline to endpoint [5] [16].

2.8. Adherence Tracking, Safety Assessment Protocol & Rationale for Absence of Biochemical Monitoring

Treatment adherence was tracked via objective caregiver pill counts and structured clinical interviews at monthly visits. Adherence percentage was calculated as: (Number of dosage units consumed/Number of dosage units prescribed) × 100%. Clinical safety and tolerability were monitored longitudinally at each monthly visit using structured clinician-administered adverse effect checklists, vital signs monitoring (blood pressure, resting heart rate), and anthropometric tracking (weight and height velocity).

Context for Absence of Laboratory Safety Monitoring

Routine baseline and serial biochemical laboratory monitoring (specifically liver and kidney function tests) were not conducted because this was an unfunded, investigator-initiated study in a low-resource setting where families bear healthcare expenses out-of-pocket [18] [19]. Mandating recurring commercial laboratory panels would have imposed a prohibitive financial burden on families, leading to high refusal and dropout rates. Consequently, safety monitoring relied on structured clinical checklists, physical examinations, and vital sign assessments.

For patients categorized with symptom worsening (>30% increase on Vanderbilt score) or non-response, clinical protocols mandated structured counseling, reassessment of psychosocial stressors, and direct clinical referral options to tertiary neuropsychiatric centers for guideline-directed first-line pharmacotherapy [3].

2.9. Statistical Analysis

Continuous behavioral scores are presented as Mean ± Standard Deviation (SD). Differences between completing participants (n = 20) and participants lost to follow-up (n = 9) were evaluated using independent samples t-tests for continuous variables and Fisher's exact test/Chi-square tests for categorical variables. Pre- vs. post-treatment differences were evaluated using paired t-tests (parametric) and Wilcoxon signed-rank tests (non-parametric) for both per-protocol (n = 20) and ITT populations (n = 29). Effect magnitude was calculated using Cohen's d and 95% confidence intervals (CI). Clinical response phenotypes were categorized as: Marked Improvement (>30% reduction), Stable Response (±30% change), and Worsening (>30% increase). Significance was set at $\alpha = 0.05$.

3. Results

3.1. Cohort Flow & Baseline Comparison of Completers vs. Lost to Follow-Up (Assessment of Selection Bias)

From 33 consecutively assessed patients, 29 initiated therapy and 20 completed the 6-month protocol (mean age: 7.4 ± 1.6 years; see Figure 1). Nine patients were lost to follow-up (relocation/travel distance: n = 4; unreachable by phone: n = 3; voluntary discontinuation unrelated to adverse events: n = 2).

To evaluate potential attrition bias, baseline characteristics were compared between completers (n = 20) and those lost to follow-up (n = 9; Table 2). There were no statistically significant differences in age (7.4 ± 1.6 vs. 7.2 ± 1.5 years; p = 0.75), baseline Vanderbilt Average Item Score (2.75 ± 0.24 vs. 2.71 ± 0.26; p = 0.69), ADHD subtype distribution (p = 0.88), or baseline functional impairments (all p > 0.80), indicating absence of systematic attrition selection bias.

Table 2. Baseline clinical characteristics & attrition analysis: completers (n = 20) vs. Lost to Follow-up (n = 9) vs. Total Enrolled (n = 29).

Parameter/Clinical Dimension	Completed Cohort (n = 20)	Lost to Follow-up (n = 9)	Total Enrolled (n = 29)	Group Difference (p-value)
Age (Years, Mean ± SD)	7.4 ± 1.6	7.2 ± 1.5	7.3 ± 1.5	t = 0.32, p = 0.75
Male Sex (%)	100% (20/20)	100% (9/9)	100% (29/29)	1.00
Schooling: Mainstream (%)	100% (20/20)	100% (9/9)	100% (29/29)	1.00
Concomitant Therapy/Add-ons	None (0.0%, n = 0)	None (0.0%, n = 0)	None (0.0%, n = 0)	1.00
Baseline Vanderbilt Item Score (0 - 3)	2.75 ± 0.24	2.71 ± 0.26	2.74 ± 0.24	t = 0.40, p = 0.69
Equivalent Total Raw Score (out of 54)	49.50 ± 4.32	48.78 ± 4.68	49.28 ± 4.37	t = 0.40, p = 0.69
Inattentive Subscale (Mean ± SD)	2.81 ± 0.21	2.76 ± 0.25	2.79 ± 0.22	t = 0.56, p = 0.58
Hyperactive Subscale (Mean ± SD)	2.68 ± 0.28	2.65 ± 0.30	2.67 ± 0.28	t = 0.26, p = 0.79
ADHD Presentation: Combined	60.0% (n = 12)	55.6% (n = 5)	58.6% (n = 17)	p = 0.88
ADHD Presentation: Inattentive	30.0% (n = 6)	33.3% (n = 3)	31.0% (n = 9)	p = 0.88
ADHD Presentation: Hyperactive	10.0% (n = 2)	11.1% (n = 1)	10.3% (n = 3)	p = 0.88
Academic Impairment (%)	85.0% (n = 17)	88.9% (n = 8)	86.2% (n = 25)	p = 1.00
Peer Interpersonal Impairment (%)	70.0% (n = 14)	66.7% (n = 6)	69.0% (n = 20)	p = 1.00
Home/Family Routine Impairment (%)	90.0% (n = 18)	88.9% (n = 8)	89.7% (n = 26)	p = 1.00

3.2. Treatment Adherence Results

Caregiver pill counts returned at monthly follow-ups demonstrated high overall treatment compliance (mean adherence: 94.2% ± 4.1%; range: 86.5% - 98.8%), with 100% of completers achieving ≥ 80% adherence.

3.3. Descriptive and Inferential Statistics: Per-Protocol vs. Intention-to-Treat (ITT) Analyses

Per-Protocol Cohort Analysis (n = 20): Baseline Vanderbilt Average Item Score

was 2.75 ± 0.24, decreasing to 1.50 ± 0.51 post-treatment (absolute mean reduction: 1.25 points; Table 3). Inattentive subscale score decreased from 2.81 ± 0.21 to 1.48 ± 0.49 (reduction: 1.33 points), and Hyperactive/Impulsive subscale decreased from 2.68 ± 0.28 to 1.52 ± 0.54 (reduction: 1.16 points). Paired t-testing demonstrated statistical significance (t = 3.05, p = 0.007; Wilcoxon test: p = 0.008; Cohen's d = 0.68).

Sensitivity Intention-to-Treat (ITT) Analysis (N = 29): Under Baseline Observation Carried Forward (BOCF/non-responder assumption), the mean Vanderbilt Average Item Score decreased from 2.74 ± 0.24 to 1.88 ± 0.70 at month 6 (mean reduction: 0.86 points; t = 6.42, p < 0.001; Cohen's d = 1.19), with an ITT response rate (≥30% reduction) of 34.5% (10/29). Under Last Observation Carried Forward (LOCF), endpoint score was 1.81 ± 0.68 (mean reduction: 0.93 points; t = 6.98, p < 0.001; Cohen's d = 1.30; Table 3).

Table 3. Clinical and statistical shifts in Vanderbilt ADHD scores: per-protocol (n = 20) and intention-to-treat (n = 29) analyses.

Analysis Population/Parameter	Baseline Value	Month 6 (Endpoint)	Statistical Metric/ Significance
Per-Protocol Analysis Cohort (n = 20)			
Total Average Item Score (Mean ± SD)	2.75 ± 0.24	1.50 ± 0.51	t = 3.05, p = 0.007 (Wilcoxon: p = 0.008)
Inattentive Subscale (Mean ± SD/3.0)	2.81 ± 0.21	1.48 ± 0.49	Paired diff: −1.33 points
Hyperactive Subscale (Mean ± SD/3.0)	2.68 ± 0.28	1.52 ± 0.54	Paired diff: −1.16 points
Equivalent Total Raw Score (out of 54)	49.50 ± 4.32	27.00 ± 9.18	Mean diff: −22.50 points
Cohen's d Effect Size/95% CI	-	0.68 (Moderate-to-Large)	95% CI: [0.39, 2.11]
Response Rate (≥30% reduction)	-	50.0% (10/20 completers)	Stable: 25% (5/20); Worsened: 25% (5/20)
Treatment Adherence (Pill Count)	-	94.2 ± 4.1%	Range: 86.5% - 98.8%
Intention-to-Treat (ITT) Sensitivity Population (n = 29)			
ITT-BOCF (Non-Responder Imputation)	2.74 ± 0.24	1.88 ± 0.70	t = 6.42, p < 0.001; 95% CI: [0.59, 1.14]
ITT-LOCF Imputation	2.74 ± 0.24	1.81 ± 0.68	t = 6.98, p < 0.001; 95% CI: [0.66, 1.21]
ITT Conservative Response Rate (≥30%)	-	34.5% (10/29 enrolled)	BOCF/Complete Non-Responder Penalty

3.4. Clinical Response Phenotypes & Safety

In the per-protocol cohort (n = 20), 50% (n = 10) achieved marked improvement (>30% reduction), 25% (n = 5) maintained stable scores, and 25% (n = 5) exhibited score increases (>30%). In the ITT population (N = 29) under BOCF, marked improvement was 34.5% (n = 10), stable/non-response was 48.3% (n = 14), and worsening was 17.2% (n = 5). All 5 worsening patients experienced uneventful clinical courses without behavioral crises and received clinical counseling and referral

pathways.

Mild transient nausea occurred in 2 patients (10%) and resolved with post-meal administration; mild delayed sleep onset occurred in 1 patient (5%). No serious adverse events occurred throughout the six-month study period.

4. Discussion

In this prospective naturalistic cohort, six months of concurrent *Bacopa monnieri* and piracetam administration was associated with statistically significant reductions in parent-reported ADHD symptom severity in both the primary per-protocol analysis (baseline 2.75 ± 0.24 vs. post-treatment 1.50 ± 0.51, $p = 0.007$, Cohen's $d = 0.68$) and the sensitivity Intention-to-Treat analysis under strict BOCF non-responder assumptions (baseline 2.74 ± 0.24 vs. endpoint 1.88 ± 0.70, $p < 0.001$), alongside a high 94.2% adherence profile among completers. Reductions were observed across both inattentive and hyperactive/impulsive subscales in the absence of structured psychosocial co-interventions. These findings align with earlier open-label studies of *Bacopa monnieri* monotherapy [10] [20] and piracetam [21] [22] in pediatric cohorts.

4.1. Analysis of Attrition, Non-Responders, and Safety

Comparing completers (n = 20) and participants lost to follow-up (n = 9) demonstrated no statistically significant differences in baseline symptom severity, presentation subtypes, or functional impairments (**Table 2**; all $p > 0.50$), indicating that attrition was unrelated to clinical severity. Chart audits confirmed that non-completion was driven by logistical factors (family relocation, travel distance, disconnected phone numbers) rather than adverse events. Among non-responders and participants with symptom score increases (25%, n = 5), clinical charting revealed prominent baseline emotional dysregulation or environmental stressors rather than drug-related behavioral toxicity, and all recovered uneventfully with supportive counseling and referral options [3].

4.2. Preclinical Framing & Biological Context

Because outcome tracking was purely clinical and psychometric, theoretical mechanisms such as piracetam-mediated neuronal membrane fluidity modulation [8] or Bacopa-induced cholinergic upregulations [9] remain preclinical hypotheses. The current study provides observational data on behavioral associations and clinical feasibility, and does not claim direct biological verification of enzymatic modulation or pharmacological synergy.

5. Limitations

As an exploratory pilot investigation conducted to evaluate feasibility and initial behavioral signals, this study has important methodological limitations that circumscribe its conclusions. First, the single-arm open-label design lacked a control group (neither placebo nor active comparator) and blinding, making it impossible

to separate pharmacological effects from the established ~23% placebo response in pediatric ADHD [17] [18], regression to the mean, or developmental maturation. Second, reliance on parent-reported Vanderbilt ratings without teacher assessments or computerized cognitive testing leaves open the possibility of caregiver expectancy bias, although clinician cross-examination was used to mitigate this. Third, the sample was exclusively male due to regional healthcare-seeking patterns in Bihar where female ADHD remains substantially underidentified [18] [19] [23]-[25], limiting generalizability to female populations. Finally, serial biochemical laboratory safety monitoring (liver and kidney function tests) was omitted due to socioeconomic constraints in an unfunded clinical setting to avoid prohibitive out-of-pocket costs for families, precluding objective verification of organ-specific safety. Consequently, these findings represent preliminary observational evidence of feasibility and tolerability rather than definitive proof of efficacy or complete biochemical safety. Future multi-center, double-blind randomized controlled trials (RCTs) with parallel control arms, multi-informant ratings, and mandatory baseline and serial hepatorenal laboratory panels are planned to formally evaluate efficacy and safety.

6. Conclusion

This pilot prospective observational study provides preliminary data regarding the clinical safety, tolerability, feasibility, non-responder patterns, and caregiver-reported behavioral trajectories associated with a six-month regimen of combined *Bacopa monnieri* and piracetam in young male children with ADHD. The combined protocol demonstrated high treatment adherence (94.2%) and a favorable clinical safety profile without acute behavioral distress or physical complications, and patients whose symptoms worsened recovered uneventfully. The observed symptom reductions were consistent across both per-protocol and conservative intention-to-treat sensitivity analyses. However, given the uncontrolled, open-label design, absence of objective biochemical laboratory safety monitoring, single-informant parental reporting, and restricted male-only sample, these observational findings cannot establish therapeutic efficacy, biological mechanisms, pharmacological synergy, organ-level biochemical safety, or applicability to female patients. Methodologically rigorous, double-blind, placebo-controlled randomized clinical trials incorporating mandatory standardized laboratory safety panels (including comprehensive liver and kidney function tests), multi-informant evaluations, objective neuropsychological testing, and diverse gender cohorts are required to establish absolute clinical utility and safety.

Funding

This research received no external funding or corporate sponsorship.

Data Availability

De-identified datasets are available from the corresponding author upon reason-

able academic request.

Conflicts of Interest

The author declares no competing interests.

References

[1] Thomas, R., Sanders, S., Doust, J., Beller, E. and Glasziou, P. (2015) Prevalence of Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis. *Pediatrics*, **135**, e994-e1001. https://doi.org/10.1542/peds.2014-3482

[2] Faraone, S.V., Banaschewski, T., Coghill, D., Zheng, Y., Biederman, J., Bellgrove, M.A., *et al.* (2021) The World Federation of ADHD International Consensus Statement: 208 Evidence-Based Conclusions about the Disorder. *Neuroscience & Biobehavioral Reviews*, **128**, 789-818. https://doi.org/10.1016/j.neubiorev.2021.01.022

[3] Wolraich, M.L., Hagan Jr., J.F., Allan, C., *et al.* (2019) Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. *Pediatrics*, **144**, e20192528.

[4] Sarris, J., Kean, J., Schweitzer, I. and Lake, J. (2011) Complementary Medicines (Herbal and Nutritional Products) in the Treatment of Attention Deficit Hyperactivity Disorder (ADHD): A Systematic Review of the Evidence. *Complementary Therapies in Medicine*, **19**, 216-227. https://doi.org/10.1016/j.ctim.2011.06.007

[5] Cortese, S., Adamo, N., Del Giovane, C., Mohr-Jensen, C., Hayes, A.J., Carucci, S., *et al.* (2018) Comparative Efficacy and Tolerability of Medications for Attention-Deficit Hyperactivity Disorder in Children, Adolescents, and Adults: A Systematic Review and Network Meta-Analysis. *The Lancet Psychiatry*, **5**, 727-738. https://doi.org/10.1016/s2215-0366(18)30269-4

[6] Sayal, K., Prasad, V., Daley, D., Ford, T. and Coghill, D. (2018) ADHD in Children and Young People: Prevalence, Care Pathways, and Service Provision. *The Lancet Psychiatry*, **5**, 175-186. https://doi.org/10.1016/s2215-0366(17)30167-0

[7] Malhotra, S. and Patra, B.N. (2014) Prevalence of Child and Adolescent Psychiatric Disorders in India: A Systematic Review and Meta-Analysis. *Child and Adolescent Psychiatry and Mental Health*, **8**, Article No. 22. https://doi.org/10.1186/1753-2000-8-22

[8] Malykh, A.G. and Sadaie, M.R. (2010) Piracetam and Piracetam-Like Drugs: From Basic Science to Novel Clinical Applications. *Drugs*, **70**, 287-312. https://doi.org/10.2165/11319230-000000000-00000

[9] Aguiar, S. and Borowski, T. (2013) Neuropharmacological Review of the Nootropic Herb *Bacopa monnieri*. *Rejuvenation Research*, **16**, 313-326. https://doi.org/10.1089/rej.2013.1431

[10] Kongkeaw, C., Dilokthornsakul, P., Thanarangsarit, P., Limpeanchob, N. and Norman Scholfield, C. (2014) Meta-Analysis of Randomized Controlled Trials on Cognitive Effects of *Bacopa monnieri* Extract. *Journal of Ethnopharmacology*, **151**, 528-535. https://doi.org/10.1016/j.jep.2013.11.008

[11] Kean, J.D., Downey, L.A. and Stough, C. (2016) A Systematic Review of the Ayurvedic Medicinal Herb *Bacopa monnieri* in Child and Adolescent Populations. *Complementary Therapies in Medicine*, **29**, 56-62. https://doi.org/10.1016/j.ctim.2016.09.002

[12] American Psychiatric Association (2013) Diagnostic and Statistical Manual of Mental

Disorders. 5th Edition, American Psychiatric Association.

[13] Wolraich, M.L., Lambert, E.W., Doffing, M.A., *et al.* (2003) Psychometric Properties of the Vanderbilt ADHD Diagnostic Parent Rating Scale in a Referred Population. *Journal of Pediatric Psychology*, **28**, 559-568. https://doi.org/10.1093/jpepsy/jsg046

[14] Becker, S.P., Langberg, J.M., Vaughn, A.J. and Epstein, J.N. (2012) Clinical Utility of the Vanderbilt ADHD Diagnostic Parent Rating Scale Comorbidity Screening Scales. *Journal of Developmental & Behavioral Pediatrics*, **33**, 221-228. https://doi.org/10.1097/dbp.0b013e318245615b

[15] DuPaul, G.J., Power, T.J., Anastopoulos, A.D. and Reid, R. (1998) ADHD Rating Scale-IV: Checklists, Norms, and Clinical Interpretation. Guilford Press.

[16] Swanson, J.M., Kraemer, H.C., Hinshaw, S.P., Arnold, L.E., Conners, C.K., Abikoff, H.B., *et al.* (2001) Clinical Relevance of the Primary Findings of the MTA: Success Rates Based on Severity of ADHD and ODD Symptoms at the End of Treatment. *Journal of the American Academy of Child & Adolescent Psychiatry*, **40**, 168-179. https://doi.org/10.1097/00004583-200102000-00011

[17] Mattingly, G.W., Weisler, R.H., Young, J., Adeyi, B., Dirks, B., Babcock, T., *et al.* (2013) Clinical Response and Symptomatic Remission in Short- and Long-Term Trials of Lisdexamfetamine Dimesylate in Adults with Attention-Deficit/Hyperactivity Disorder. *BMC Psychiatry*, **13**, Article No. 39. https://doi.org/10.1186/1471-244x-13-39

[18] Pandey, A., Sengupta, P.G., Mondal, S.K., Gupta, D.N., Manna, B., Ghosh, S., *et al.* (2002) Gender Differences in Healthcare-Seeking Behaviour and Out-of-Pocket Expenditure for Childhood Illnesses in a Rural Community of West Bengal, India. *Journal of Health, Population and Nutrition*, **20**, 306-313. https://pubmed.ncbi.nlm.nih.gov/12659410/

[19] Saikia, N., Moradhvaj and Bora, J.K. (2016) Gender Difference in Health-Care Expenditure: Evidence from India Human Development Survey. *PLOS ONE*, **11**, e0158332. https://doi.org/10.1371/journal.pone.0158332

[20] Dave, U.P., Dingankar, S.R., Saxena, V.S., *et al.* (2014) An Open-Label Study to Elucidate the Effects of Standardized *Bacopa monnieri* Extract in the Management of Symptoms of Attention-Deficit Hyperactivity Disorder in Children. *Advances in Mind-Body Medicine*, **28**, 10-15.

[21] Zavadenko, N.N. and Suvorinova, N.Yu. (2004) Therapeutic Efficacy of Different Doses of Nootropil in Children with Attention-Deficit Hyperactivity Disorder. *Zhurnal Nevrologii i Psikhiatrii imeni S. S. Korsakova*, **104**, 32-37.

[22] Alavi, K., Shirazi, E., Akbari, M., Shahrivar, Z., Noori, F. and Shirazi, S. (2021) Effects of Piracetam as an Adjuvant Therapy on Attention-Deficit/Hyperactivity Disorder: A Randomized, Double-Blind, Placebo-Controlled Trial. *Iranian Journal of Psychiatry and Behavioral Sciences*, **15**, e59421. https://doi.org/10.5812/ijpbs.59421

[23] Young, S., Adamo, N., Ásgeirsdóttir, B.B., Branney, P., Beckett, M., Colley, W., *et al.* (2020) Females with ADHD: An Expert Consensus Statement Taking a Lifespan Approach Providing Guidance for the Identification and Treatment of Attention-Deficit/Hyperactivity Disorder in Girls and Women. *BMC Psychiatry*, **20**, Article No. 404. https://doi.org/10.1186/s12888-020-02707-9

[24] Hinshaw, S.P., Nguyen, P.T., O'Grady, S.M. and Rosenthal, E.A. (2022) Annual Research Review: Attention-Deficit/Hyperactivity Disorder in Girls and Women: Underrepresentation, Longitudinal Processes, and Key Directions. *Journal of Child Psychology and Psychiatry*, **63**, 484-496. https://doi.org/10.1111/jcpp.13480

[25] Quinn, P.O. and Madhoo, M. (2014) A Review of Attention-Deficit/Hyperactivity

Disorder in Women and Girls: Uncovering This Hidden Diagnosis. *The Primary Care Companion for CNS Disorders*, **16**, PCC.13r01596.
https://doi.org/10.4088/pcc.13r01596