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Bibliometric Analysis of Research on Premature Adrenarche from 1974 to 2024

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Abstract

BACKGROUND/AIMS: Premature adrenarche (PA) is a clinical condition marked by early activation of adrenal androgens prior to puberty. Once regarded as a benign developmental variant, PA is now linked to long-term health risks such as metabolic syndrome, polycystic ovary syndrome (PCOS), and type 2 diabetes. This study aims to provide a comprehensive bibliometric analysis of scientific literature on PA published between 1974 and 2024.

MATERIALS AND METHODS: This descriptive bibliometric analysis included 445 publications indexed in the Scopus database under the search term "PA". Publications were categorized by type, discipline, country, and institution. VOS viewer software was used to map keyword co-occurrence and citation networks to identify research trends and influential works.

RESULTS: Of all publications, 68.08% were original articles, 18.42% were reviews, and the remainder were book chapters or conference proceedings. The United States led with 186 publications, while Kuopio University Hospital emerged as the most prolific institution. The most frequently used keywords included "human," "child," and "adrenarche," with "DHEAS" and "androgen" reflecting growing biochemical focus. The most-cited publication was a position statement addressing PCOS.

CONCLUSION: Although there has been a notable rise in PA-related research over the last five decades, key gaps remain, particularly concerning diagnostic standardization, long-term outcomes, and underrepresentation of developing countries. Interdisciplinary approaches, harmonized diagnostic protocols, and the integration of advanced technologies will be critical to improve research quality and clinical care. This bibliometric analysis offers a valuable roadmap for future research in this evolving domain of pediatric endocrinology.

Keywords: Premature adrenarche, bibliometric analysis, citation analysis, keyword analysis, scientific mapping

INTRODUCTION

Premature adrenarche (PA) is a clinical condition resulting from early activation of the adrenal cortex, typically before 8 years of age in girls and 9 years of age in boys. It is characterized by increased secretion of adrenal androgen precursors, particularly dehydroepiandrosterone (DHEA) and its sulfate (DHEAS). Clinically, PA manifests with signs such as pubic or axillary hair development, oily skin, and acne. Fuller Albright first mentioned adrenal changes associated with early hormonal activity in 1947 in relation to osteoporosis.[1] In 1952, Silverman, Migeon, Rosemberg, and Wilkins described the appearance of sexual hair in the absence of other secondary sexual traits, coining the term "premature pubarche" and suggesting that it may represent a constitutional variant of puberty.[2]

Initially considered a benign variation of normal development, PA may, according to subsequent research, serve as a precursor to more serious conditions such as metabolic syndrome (MetS), polycystic ovary syndrome (PCOS), and type 2 diabetes.[3,4] A central aspect of the pathophysiology of PA is the premature development of the adrenal zona reticularis, resulting in incomplete enzymatic maturation-especially of 3β-hydroxysteroid dehydrogenase-and subsequent

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increased production of DHEA and DHEAS.[5,6] Morphological studies of the adrenal cortex support this mechanism, showing a specific structural differentiation of the zona reticularis during adrenarche.[6]

Moreover, elevated DHEAS levels during PA have been recognized not merely as a transient biochemical variation but also as a potential biomarker for long-term endocrine and metabolic disturbances.[7] PA is thus increasingly viewed as a multifactorial syndrome influenced by genetic, intrauterine, and environmental factors.[8] For instance, Ibáñez et al.[4] and colleagues demonstrated that girls born small for gestational age were at increased risk of PA, hyperinsulinemia, and subsequent ovarian hyperandrogenism. This supports the concept of fetal programming, where early growth restriction and compensatory postnatal insulin secretion contribute to adrenal hyperfunction.[9]

Children with PA also display an increased risk for obesity, insulin resistance, and lipid abnormalities, all of which are components of MetS.[10,11] Akinci et al.[12] and colleagues observed that young women with a history of PA had a significantly higher prevalence of MetS, supporting the hypothesis that PA is not simply a transient variation in development but a marker of systemic risk. These hormonal alterations may influence multiple regulatory pathways, ultimately increasing the risk of cardiovascular disease and type 2 diabetes in adulthood.[13,14]

PA is also associated with accelerated linear growth and advanced bone age during childhood. Utriainen et al.[15] found that girls with PA had significantly faster height velocity in early childhood, often resulting in compromised final height due to early epiphyseal fusion. Similarly, Ghizzoni and Milani[16] described PA as a natural variant of adrenarche with variable outcomes depending on individual metabolic and hormonal contexts.

As the clinical implications of PA have broadened, so too has the scientific interest in this condition. The volume of research has grown considerably in recent decades, necessitating a structured evaluation of trends in publication activity and thematic development. Bibliometric analysis provides a powerful methodological framework for mapping scientific landscapes, identifying influential studies, authors, institutions, and research clusters.[17-19]

In this study, we conducted a bibliometric analysis of 445 articles indexed in Scopus from 1974 to 2024 using the keyword "PA." The objective was to systematically examine the growth trajectory of PA-related literature, identify high-impact studies and collaborative networks, and analyze thematic clusters addressing etiology, clinical outcomes, genetic factors, and environmental factors. Through this structured approach, we aim to offer a comprehensive overview of scientific progress in PA and outline a roadmap for future research.[20-25]

MATERIALS AND METHODS

This study was conducted as a bibliometric analysis of previously published studies, and, as it does not involve human participants, an opinion was obtained from the Hitit University Ethics Committee stating that ethical committee approval was not required (02.07.2025; 2024/1974-2024).

This study utilized a bibliometric analysis approach to systematically examine the research landscape on PA between 1974 and 2024. Bibliometric analysis is a quantitative method used to evaluate scientific publications by measuring productivity, impact, and collaboration patterns within a specific research field. In this context, the method enables the identification of publication trends, influential authors, and thematic structures through citation data and keyword relationships. All bibliographic information was retrieved from the Scopus (Elsevier) database and analyzed using standard bibliometric indicators.

Statistical Analysis

All retrieved data were analyzed using descriptive statistical methods. Frequency and percentage distributions were calculated to summarize publication characteristics such as document type, publication year, and country of origin. Bibliometric mapping and visualization were performed using VOSviewer (version 1.6.20) to generate co-authorship, co-citation, and keyword co-occurrence networks. These maps were used to illustrate the intellectual and collaborative structure of the field. Data cleaning, tabulation, and graph generation were conducted in Microsoft Excel 2024. All analyses were descriptive in nature, and no inferential statistical tests were applied.

RESULTS

A total of 445 publications related to PA were identified in the Scopus database. The data revealed that the highest number of publications was recorded in 2024, with 22 studies. This was followed by 2012, 2015, 2022, and 2023 (each with 20 publications), and by 2017, 2018, and 2020 (each with 19 publications). Among these, 303 studies (68.08%) were journal articles, 82 (18.42%) were review articles, 26 (5.84%) were book chapters, 16 (3.59%) were conference papers, and 7 (1.57%) were letters (Table 1).

Active Institutions

In the field of PA, the most active institution was Kuopio University Hospital, with 29 publications. This was followed by Itä-Suomen Yliopisto, which contributed 27 publications (Table 2).

Active Journals

In the field of PA, the most prolific journal was the Journal of Clinical Endocrinology and Metabolism, which published 44 studies. It was followed by the Journal of Pediatric Endocrinology and Metabolism, which had 31 publications (Table 3).

Active Countries

In the field of PA, the United States was the most prominent contributor, with a total of 186 publications. This was followed by the United Kingdom, with 36 publications, and Finland, with 34 publications (Figures 1 and 2).

Table 1. Distribution of publications

	Number of publications	Percentage
Article	303	68.1%
Review	82	18.4%
Book chapter	26	5.8%
Conference paper	16	3.6%
Letter	7	1.6%
Note	4	0.9%
Editorial	4	0.9%
Short survey	3	0.7%
Total	445	100%

Most Cited Publications

The most cited study in the field of PA was "The polycystic ovary syndrome: A position statement from the European Society of Endocrinology," which received 544 citations.[26] This was followed by "Prader-Willi syndrome," cited 493 times,[27] and "Public health implications of altered puberty timing," with 403 citations (Table 4).[28]

Research Areas with the Most Publications

The field of medicine accounted for the largest number of studies on PA, with a total of 411 publications. This was followed by biochemistry, genetics, and molecular biology, which encompassed 219 studies, and by neuroscience, which encompassed 8 studies (Figure 3).

Keyword Analysis and Trending Topics

A total of 801 keywords were identified across 445 publications extracted from the Scopus database spanning the years 1974 to 2024. Among these, 37 keywords were utilized in at least five publications. Network visualizations based on these keywords were presented in Figure 4. The visualizations revealed that prominent keywords were "human," "female," "adrenarche," and "child." In recent years, "DHEAS," "androgen," and "adrenarche" have emerged as prominent topics indicating a growing focus on these areas (Figure 4).

Table 2. Active institutions

Affiliation	Research numbers
Kuopio University Hospital	29
Itä-Suomen yliopisto	27
UPMC Children's Hospital of Pittsburgh	14
Montefiore Medical Center	13
Albert Einstein College of Medicine	13
University of California, San Francisco	12
National and Kapodistrian University of Athens	12
Helsingin Yliopisto	11
Aghia Sophia Children's Hospital	11
Rigshospitalet	11
Universidad de Chile	10
Columbia University	10
School of Medicine	10

Table 3. Active journals

Active journals	Research numbers
Journal of Clinical Endocrinology and Metabolism	44
Journal of Pediatric Endocrinology and Metabolism	31
Hormone Research in Paediatrics	19
Clinical Endocrinology	13
Journal of Pediatrics	10
Frontiers in Endocrinology	10
Pediatric Research	8
European Journal of Endocrinology	7
Hormone Research	7
Journal of the Endocrine Society	6
Endocrinologist	5
Pediatrics	5
Pediatric Endocrinology Reviews	5
European Journal of Pediatrics	5

Thematic Content of Frequently Cited Studies

The content of the most frequently cited publications revealed key thematic focuses in PA research, including clinical presentation (e.g., early pubarche, growth patterns), hormonal evaluation (e.g., DHEA-S, androstenedione), imaging findings, differential diagnosis (e.g., congenital adrenal hyperplasia, PCOS), and psychosocial implications. These topics were predominantly observed in studies published after 2000, indicating an increasingly interdisciplinary approach.

DISCUSSION

This bibliometric analysis, covering a 50-year span from 1974 to 2024, systematically examined the scientific landscape surrounding PA, revealing important academic trends and critical gaps in the literature. The findings highlighted the dominance of clinical disciplines, geographical disparities in research output, evolving thematic focuses, and emergent directions for future inquiry.

Dominance of Medical Research in Premature Adrenarche Studies

A striking majority of the literature on PA (411 of 445 publications) originated within the medical field, reflecting its central relevance to pediatric endocrinology and metabolic health. This concentration underscores the clinical framing of PA as a disorder with diagnostic and therapeutic implications. However, contributions from fields such as neuroscience, molecular biology, and psychology remain sparse, leaving significant gaps in our understanding of the neuroendocrine mechanisms and psychosocial outcomes associated with PA. For instance, according to the World Health Organization (WHO), insulin resistance and early-onset MetSs often originate in childhood neuroendocrine dysregulation, indicating the need for a broader, interdisciplinary approach to comprehensively investigate PA.

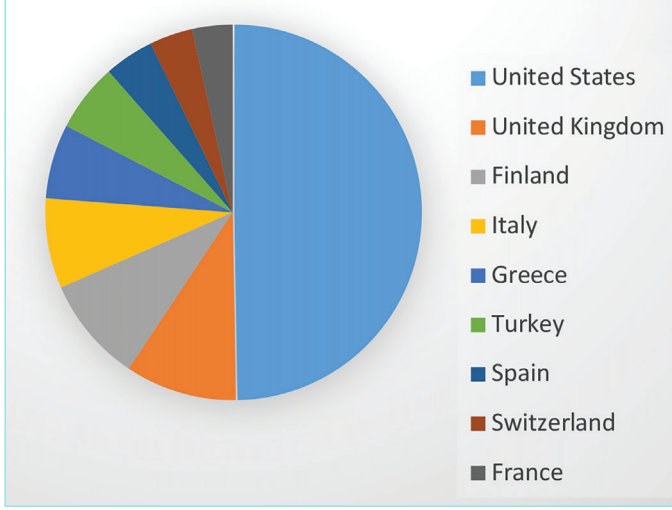

Figure 1. Active countries.

Geographical Trends and Research Leadership

The United States led the global research effort with 186 publications, likely reflecting its extensive biomedical research infrastructure. The United Kingdom (36 publications) and Finland (34 publications) followed, with notable contributions from institutions such as Kuopio University Hospital and the University of Eastern Finland.

The prominent role of Finland suggests the effectiveness of focused national research funding in driving output in niche fields. Conversely, the limited participation from developing countries may reflect disparities in research resources and collaboration networks. This imbalance underscores the importance of promoting global equity in research by supporting underrepresented regions.

Publication Types and Citation Patterns

Analysis revealed that 68% of the PA literature were original research articles, while 18% were review articles, indicating both active data generation and a growing interest in synthesizing existing knowledge. Foundational contributions such as Conway et al.[26] study on PCOS-cited over 500 times-demonstrate how PA intersects with broader endocrinological disorders like MetS and reproductive dysfunctions.[6] Such high-impact publications serve as intellectual anchors within the field and shape subsequent research directions.

Keyword Dynamics and Emerging Themes

Keyword analysis indicated that the most frequently used terms were

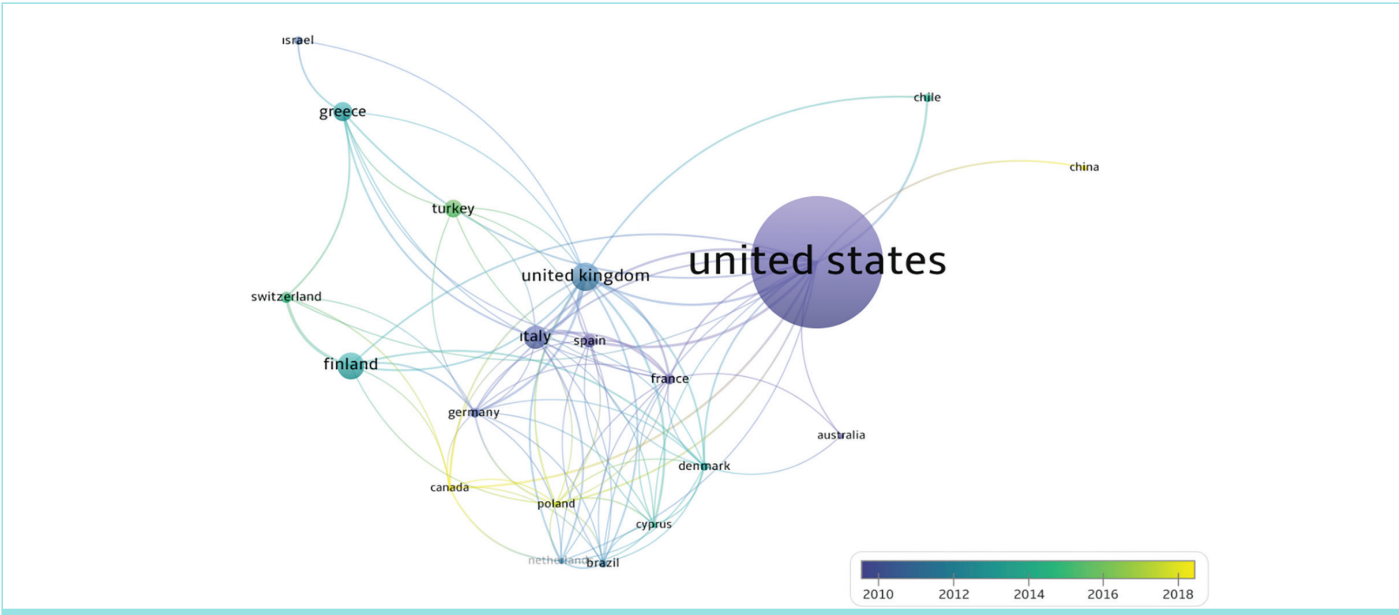

Figure 2. Active countries by year and the research intensity of countries.

Table 4. Most cited publications

Article	Authors	Source	Citations
The polycystic ovary syndrome: A position statement from the European Society of Endocrinology	Conway et al.[26]	European Journal of Endocrinology	544
Prader-Willi syndrome	Cassidy et al.[27]	European Journal of Human Genetics	493
Public health implications of altered puberty timing	Golub et al.[28]	Pediatrics	403
Premature adrenarche - Normal variant or forerunner of adult disease?	Ibáñez et al.[5]	Endocrine Reviews	376
Diagnosis and management of Silver-Russell syndrome: First international consensus statement	Wakeling et al.[29]	Nature Reviews Endocrinology	367
Clinical review: Identifying children at risk for polycystic ovary syndrome	Rosenfield[30]	Journal of Clinical Endocrinology and Metabolism	245
Adrenarche - Physiology, biochemistry and human disease	Auchus and Rainey[31]	Clinical Endocrinology	242
Short-term and long-term sequelae in intrauterine growth retardation	Longo et al.[32]	Journal of Maternal-Fetal and Neonatal Medicine	224
Hormonal changes in puberty III: Correlation of plasma dehydroepiandrosterone, testosterone, FSH, and LH with stages of puberty and bone age in normal boys and girls and in patients with addison's disease or hypogonadism or with premature or late adrenarche	Sizonenko and Paunier[33]	Journal of Clinical Endocrinology and Metabolism	181
The rise in adrenal androgen biosynthesis:Adrenarche	Havelock et al.[34]	Seminars in Reproductive Medicine	144

FSH: Follicle-stimulating hormone, LH: Luteinizing hormone.

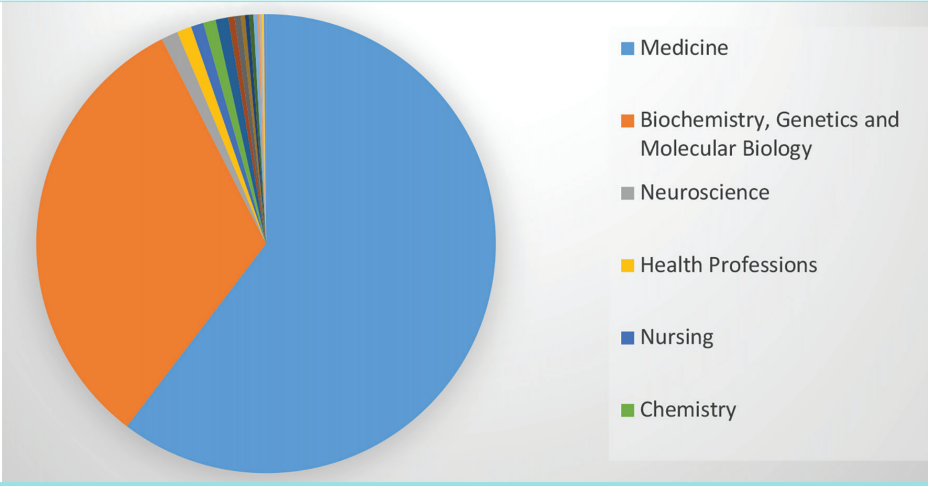

Figure 3. Research areas with the most publications.

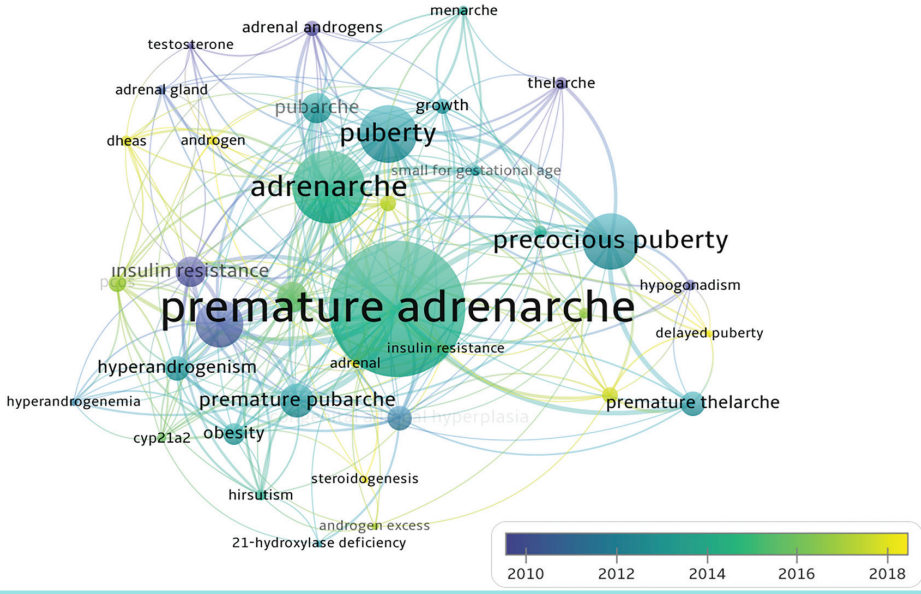

Figure 4. Network visualization of the most frequently used keywords.

"human," "child," and "adrenarche," underscoring the clinical and demographic focus of the literature. In parallel, emerging biochemical themes, such as DHEAS and androgens, reflect a heightened interest in the hormonal biomarkers of PA. The emergence of COVID-19 among the trending keywords also suggests an evolving contextualization of PA in relation to recent environmental and societal stressors. This shift aligns with growing research on how the pandemic has influenced pediatric endocrine disorders through altered routines, stress, and diet.[7,8]

Gaps in the Literature and Future Research Directions

Despite substantial advancements, significant gaps persist in the PA literature. Most notably, the long-term health outcomes of individuals with a history of PA remain poorly documented. While several cross-sectional studies have linked PA to increased risks of insulin resistance, abdominal obesity, dyslipidemia, and type 2 diabetes in later life,[4,8,10,13,14,35-37] these findings are based on limited follow-up data. The need for long-term, prospective cohort studies is urgent. According to WHO reports, early-onset metabolic and endocrine conditions, such as PA, may predispose individuals to lifelong health risks. However, the literature remains limited in establishing direct connections between childhood PA and adult cardiovascular morbidity, hypertension, or psychiatric comorbidities.

The neuroendocrine and psychosocial consequences of PA are similarly under-researched. The effects of early androgen exposure on emotional regulation, behavior, and cognitive development remain poorly understood.[3,37-39] The possible interaction between elevated DHEAS levels and the GABAergic system in the brain calls for interdisciplinary investigations combining endocrinology, psychiatry, and neuroscience.

Diagnostic variability also poses a barrier to clinical standardization. Many studies rely solely on clinical signs and DHEAS measurements to define PA, yet these parameters can vary with age, pubertal status, ethnicity, and environmental influences.[5,6,40-42] There is a critical need for

consensus-based diagnostic criteria and age-specific reference ranges.

Moreover, therapeutic approaches to PA remain ambiguous. Often dismissed as a benign developmental variant, PA is rarely targeted for early intervention. Yet, accumulating evidence suggests that early metabolic or hormonal interventions may yield long-term benefits in selected cases.[12,25,43] Multicenter randomized controlled trials are therefore essential to evaluate the efficacy and safety of such interventions.

Future research on PA should prioritize several strategic directions to address the current gaps in knowledge. First, genetic and epigenetic profiling must be advanced, particularly through studies that investigate polymorphisms in steroidogenesis-related genes such as *CYP21A2* and *CYP11B1*, which may clarify the genetic underpinnings of PA.[44,45] Second, the emerging role of gut microbiota in endocrine function suggests that longitudinal studies are warranted to explore the relationship between PA, microbial dysbiosis, and chronic systemic inflammation.[46,47] Third, the application of artificial intelligence and advanced data modeling holds promise for refining early diagnostic tools and improving risk stratification. Machine learning techniques, leveraging large datasets, could facilitate the development of predictive algorithms for early PA detection and prognosis.[20,24,48] Fourth, given the suspected neuroendocrine effects of early androgen exposure, psychological and cognitive assessments should be incorporated into longitudinal cohort studies. These would help elucidate potential neurodevelopmental consequences of PA using validated cognitive and behavioral instruments.[37,39] Lastly, the establishment of global, multicenter collaborative research networks is essential. Such networks would not only allow for more comprehensive and diverse data collection but also promote equity in scientific representation, ensuring that findings are generalizable across geographic and socioeconomic boundaries. In sum, future research on PA must evolve toward a more integrative, multidisciplinary, and globally inclusive framework. Such an approach will not only deepen our understanding of PA's complex etiology but also improve clinical practices, early detection, and prevention strategies across diverse populations.

Study Limitations

While this study provides a comprehensive overview of the scientific literature on PA, certain limitations should be acknowledged to ensure transparency. The analysis was based exclusively on records indexed in the Scopus database, which may not fully represent publications listed in other databases such as PubMed or Web of Science. As with all bibliometric studies, the results reflect patterns of publication and citation rather than the qualitative depth of the research content. Nevertheless, the use of a major, multidisciplinary database such as Scopus and the application of established bibliometric tools (VOSviewer) provide a robust and representative view of global research activity in this field. Future studies may further enhance these findings by incorporating multiple databases or by integrating bibliometric mapping with qualitative content analyses.

CONCLUSION

This bibliometric analysis of 445 publications on PA over the past five decades reveals a growing but uneven body of research, largely concentrated in developed countries and primarily within pediatric endocrinology. Despite emerging evidence linking PA to long-term risks such as MetS, insulin resistance, and PCOS, the literature is limited by inconsistent diagnostic criteria, scarce longitudinal data, and minimal interdisciplinary integration. Future studies should adopt harmonized methodologies, include underrepresented populations, and explore emerging areas such as neuropsychological outcomes, genetic and epigenetic factors, and AI-driven analytics. A multidimensional and globally inclusive approach is essential to advance clinical care and long-term health outcomes related to PA.

MAIN POINTS

- This study presents the first comprehensive bibliometric analysis of premature adrenarche (PA) research covering the period 1974-2024, encompassing 445 publications indexed in the Scopus database.
- The analysis identified a steady increase in publication activity over the last two decades, with the United States, United Kingdom, and Finland emerging as leading contributors.
- Keyword co-occurrence and citation network analyses revealed key research foci concerning dehydroepiandrosterone sulfate, androgens, and metabolic outcomes, reflecting a growing biochemical and clinical orientation.
- The findings highlight persistent gaps in diagnostic standardization, long-term follow-up studies, and contributions from developing countries.
- This study provides a quantitative foundation and research roadmap for future interdisciplinary investigations into the pathophysiology, diagnosis, and long-term outcomes of PA.

ETHICS

Ethics Committee Approval: This study was conducted as a bibliometric analysis of previously published studies, and, as it does not involve human participants, an opinion was obtained from the Hitit University Ethics Committee stating that ethical committee approval was not required (02.07.2025; 2024/1974-2024).

Informed Consent: Not applicable, as this study is a bibliometric analysis of previously published literature.

DISCLOSURES

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