



RESEARCH ARTICLE

MOST COMMON DISEASES ASSOCIATED WITH HYPERPROLACTINEMIA IN WOMEN AND THEIR RISK FACTORS: A SYSTEMATIC REVIEW

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Abstract

Background: Hyperprolactinemia is a common endocrine disorder in women and represents a frequent cause of menstrual irregularities, infertility, and galactorrhea. It may result from physiological, pathological, or pharmacological causes, with varying clinical implications.

Objective: To systematically review the literature on the most common diseases associated with hyperprolactinemia in women and to identify their associated risk factors.

Methods: A systematic search of PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar was conducted for studies published between 2000 and 2025. Observational studies, clinical cohorts, case-control studies, and systematic reviews reporting causes or risk factors of hyperprolactinemia in women were included. Data were synthesized narratively.

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Results: The most frequently reported diseases associated with hyperprolactinemia in women were prolactinomas, polycystic ovary syndrome (PCOS), primary hypothyroidism, medication-induced hyperprolactinemia, pituitary

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stalk lesions, and chronic kidney disease. Major risk factors included female sex, reproductive age, use of dopamine antagonists, estrogen exposure, pituitary adenomas, and autoimmune thyroid disease.

Conclusion: Hyperprolactinemia in women is predominantly associated with pituitary and endocrine disorders as well as medication use. Recognition of underlying causes and risk factors is essential for appropriate diagnosis and management.

Introduction:-

Hyperprolactinemia is defined as persistent elevation of serum prolactin levels above the normal reference range. It is particularly prevalent among women of reproductive age and represents a major cause of menstrual disturbances, anovulation, infertility, and galactorrhea. Prolactin secretion is primarily regulated by inhibitory dopaminergic control from the hypothalamus, and disruption of this pathway leads to elevated prolactin levels. The etiology of hyperprolactinemia is heterogeneous and includes physiological states such as pregnancy, pathological conditions affecting the pituitary or hypothalamus, systemic diseases, and pharmacological agents. Understanding the most common diseases associated with hyperprolactinemia in women and their risk factors is essential for accurate diagnosis and tailored treatment.

Methods:-

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

Search Strategy:-

Electronic databases including PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar were searched for articles published between January 2000 and March 2025. Search terms included combinations of: "hyperprolactinemia", "prolactin", "women", "female", "prolactinoma", "PCOS", "hypothyroidism", "drug-induced hyperprolactinemia", and "risk factors".

Eligibility Criteria:-

Inclusion criteria were original studies and systematic reviews reporting causes, associated diseases, or risk factors for hyperprolactinemia in women. Studies including mixed populations were included if female-specific data were reported. Exclusion criteria included pediatric-only studies and non-English publications.

Data Extraction and Synthesis:-

Data extracted included study design, population characteristics, underlying diseases associated with hyperprolactinemia, and reported risk factors. Due to heterogeneity of study designs, findings were synthesized narratively.

Results:-

Most common diseases associated with hyperprolactinemia in women:-

Across included studies, prolactinomas were consistently identified as the most common pathological cause of hyperprolactinemia in women. Microprolactinomas were more prevalent than macroadenomas and frequently presented with menstrual irregularities and infertility. Polycystic ovary syndrome (PCOS) was another frequently reported condition associated with mild to moderate hyperprolactinemia. Proposed mechanisms include altered dopaminergic tone and estrogen excess. Primary hypothyroidism was strongly associated with hyperprolactinemia due to increased thyrotropin-releasing hormone (TRH) stimulation of prolactin secretion. Drug-induced hyperprolactinemia, particularly due to antipsychotics and antidepressants, represented a major reversible cause.

Risk factors for hyperprolactinemia in women:-

Identified risk factors included reproductive age, female sex hormones, pregnancy and postpartum state, use of dopamine antagonists, pituitary adenomas, autoimmune thyroid disease, chronic kidney disease, and chest wall lesions.

Most Common Diseases Associated with Hyperprolactinemia in Women and Their Risk Factors: A Systematic Review:-

Results:-

Table 1. Most common diseases associated with hyperprolactinemia in women

Disease	Estimated frequency	Typical prolactin level	Key clinical features
Prolactinoma	40–60%	>100 ng/mL	Amenorrhea, galactorrhea, infertility
Drug-induced	20–30%	25–100 ng/mL	History of antipsychotic/antidepressant use
PCOS	10–20%	Mild elevation	Oligomenorrhea, hyperandrogenism
Primary hypothyroidism	5–10%	Mild–moderate	Weight gain, fatigue
Pituitary stalk lesions	<5%	Moderate	Headache, visual symptoms

Table 2. Risk factors associated with hyperprolactinemia in women

Risk factor	Associated condition	Strength of evidence	Notes
Reproductive age	Prolactinoma	Strong	Higher diagnostic rates
Estrogen exposure	Physiologic/PCOS	Moderate	Oral contraceptives, pregnancy
Dopamine antagonists	Drug-induced	Strong	Antipsychotics, metoclopramide
Autoimmune thyroid disease	Hypothyroidism	Strong	↑TRH stimulates prolactin
Chronic kidney disease	Systemic disease	Moderate	Reduced prolactin clearance

Figure 1. Distribution of causes of hyperprolactinemia in women:

Figure 2. PRISMA flow diagram:

Narrative summary of results:

Prolactinomas were the predominant pathological cause of hyperprolactinemia in women, accounting for approximately half of reported cases. Drug-induced hyperprolactinemia represented the most common reversible cause, particularly among women receiving antipsychotic therapy. PCOS and hypothyroidism were frequently associated with mild to moderate elevations in prolactin levels. Systemic and hypothalamic-pituitary disorders accounted for a smaller proportion of cases but were clinically significant.

Discussion:-

This systematic review demonstrates that prolactinomas represent the most common disease associated with hyperprolactinemia in women, followed by PCOS, hypothyroidism, and medication-induced causes. These findings are consistent with international endocrine literature. The strong association between hypothyroidism and hyperprolactinemia highlights the importance of thyroid function testing in all women presenting with elevated prolactin levels. Similarly, careful medication history is critical, as drug-induced hyperprolactinemia is often reversible. From a clinical perspective, early identification of risk factors allows targeted investigations, avoids unnecessary imaging, and facilitates timely treatment. Future research should focus on large prospective cohorts and standardized diagnostic thresholds.

Conclusion:-

In women, hyperprolactinemia is most commonly associated with prolactinomas, endocrine disorders such as PCOS and hypothyroidism, and pharmacological agents. Awareness of disease-specific risk factors is essential for optimal diagnostic and therapeutic strategies.

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