INPLASY

Endocrine Adverse Effects of Selective Serotonin Reuptake Inhibitors: A Systematic Review of Galactorrhea and Hyperprolactinemia

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ADMINISTRATIVE INFORMATION

Support - No specific external funding was received. This study is conducted as part of academic research activities at Taif University.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 May 2026 and was last updated on 17 May 2026.

INTRODUCTION

Review question / Objective This systematic review aims to evaluate the clinical characteristics, implicated SSRIs, prolactin abnormalities, latency periods, management approaches, and outcomes of galactorrhea and/or hyperprolactinemia associated with selective serotonin reuptake inhibitors. The review includes patients exposed to SSRIs who developed endocrine adverse effects reported in case reports and case series.

Rationale Selective serotonin reuptake inhibitors are among the most commonly prescribed psychotropic medications and are generally considered safe and well tolerated. However, accumulating evidence from case reports suggests that SSRIs may alter prolactin regulation and induce galactorrhea and/or hyperprolactinemia. These endocrine adverse effects remain underrecognized and may negatively affect quality of life, treatment adherence, reproductive health, and psychosocial functioning. Existing evidence remains fragmented across isolated reports without comprehensive synthesis. Therefore, this review was conducted to systematically summarize the available evidence regarding clinical presentation, implicated medications, prolactin abnormalities, management strategies, and outcomes of SSRI-associated galactorrhea and hyperprolactinemia.

Condition being studied Galactorrhea and hyperprolactinemia associated with selective serotonin reuptake inhibitor therapy. Galactorrhea refers to inappropriate milk secretion unrelated to pregnancy or lactation, while hyperprolactinemia refers to elevated serum prolactin levels. These endocrine adverse effects may occur during SSRI treatment and may be associated with breast symptoms, menstrual disturbances, infertility concerns, or psychosocial distress.

METHODS

Search strategy A systematic search was conducted in PubMed, Scopus, and Web of

Science from database inception to June 2025. Search terms included combinations of "Selective serotonin reuptake inhibitors", "SSRI", "Fluoxetine", "Paroxetine", "Sertraline", "Escitalopram", "Citalopram", "Fluvoxamine", "Galactorrhea", "Hyperprolactinemia", and "Prolactin". Both keywords and MeSH terms were used where applicable. Reference lists of included studies were manually screened for additional relevant reports.

Participant or population Patients of any age or sex who developed galactorrhea and/or hyperprolactinemia during treatment with selective serotonin reuptake inhibitors.

Intervention Exposure to selective serotonin reuptake inhibitors including fluoxetine, paroxetine, sertraline, escitalopram, citalopram, and fluvoxamine.

Comparator Not applicable.

Study designs to be included Published case reports and case series reporting galactorrhea and/or hyperprolactinemia associated with selective serotonin reuptake inhibitor therapy.

Eligibility criteria Included studies were human case reports and case series describing galactorrhea and/or hyperprolactinemia associated with SSRIs. Reviews, editorials, animal studies, observational studies without patient-level data, and reports with unclear causality or alternative definitive causes of hyperprolactinemia were excluded.

Information sources PubMed, Scopus, and Web of Science databases were searched. Manual screening of reference lists from included studies was also performed to identify additional eligible publications.

Main outcome(s) The main outcomes include occurrence of galactorrhea and/or hyperprolactinemia following SSRI exposure, serum prolactin levels, timing of symptom onset, and symptom resolution after management or medication discontinuation.

Additional outcome(s) Additional outcomes include amenorrhea, breast tenderness, breast enlargement, implicated SSRI type and dose, recurrence after rechallenge, follow-up duration, and management strategies.

Data management Retrieved records were imported into Rayyan software for screening and duplicate removal. Data extraction was performed using a standardized Excel-based form including demographics, psychiatric diagnosis, SSRI type and dose, prolactin levels, symptom onset, management, and outcomes.

Quality assessment / Risk of bias analysis The methodological quality of included studies was assessed using the Joanna Briggs Institute critical appraisal tools for case reports and case series.

Strategy of data synthesis Due to the descriptive nature and heterogeneity of included studies, a narrative synthesis approach was used. Findings were summarized in tables and analyzed according to clinical characteristics, implicated SSRIs, prolactin findings, latency periods, management strategies, and outcomes.

Subgroup analysis Narrative subgroup comparisons were conducted according to SSRI type, sex, age group, prolactin level status, symptom onset timing, and management strategy.

Sensitivity analysis Sensitivity analysis was not applicable because quantitative meta-analysis was not performed.

Language restriction English-language studies only.

Country(ies) involved Saudi Arabia.

Other relevant information This protocol is retrospectively registered for transparency purposes. The review was conducted in accordance with PRISMA principles and used JBI appraisal tools for methodological assessment.

Keywords SSRIs; Galactorrhea; Hyperprolactinemia; Prolactin.

Dissemination plans The findings of this review will be submitted to a peer-reviewed psychiatry or psychopharmacology journal and may be presented at scientific conferences.

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