

Review Article



Impact of Oral Contraceptive Use for Religio - Cultural Practices on Cerebral Venous Thrombosis Risk in Women: A Systematic Review and Meta-Analysis

Lakshmi Priya. A¹, Shyam Sundar. S¹, Padma Priya. A¹, Kaushik. K¹, Dr. Dhivya. K^{*2}

1 Pharm. D student, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, India.

2 Assistant Professor, Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, India.

*Corresponding author's E-mail: divyapharmd@gmail.com

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ABSTRACT

Background: "Pregnancy and fertility are not diseases; they are natural physiological processes., but labelling them as medical conditions enables contraception to be framed as a "cure". Many women use OCs to delay menstruation due to religious restrictions, facing social exclusion. Unregulated OC use raises concerns about thromboembolic risks.

Purpose: This study aims to evaluate the impact of OC use on thromboembolic event risk in women in context of religio-cultural practices. It seeks to highlight public health implications and promote safer contraceptive and menstrual management strategies.

Methodology: This systematic review and meta-analysis followed PRISMA guidelines, analysing literature up to 2024. A total of 31 studies were included, comprising 19 for the systematic review and 12 for the meta-analysis, assessing the association between oral contraceptive use and thromboembolic event risk. A comprehensive search was conducted across PubMed, ScienceDirect, and Google Scholar.

Results: The systematic review included 1,072 patients (mean age 32.72 ± 7.71 years) using OCPs for religious reasons, with MRI/MRV as primary diagnostic tools. The meta-analysis of 12 studies found a significant association between hormonal contraceptive use and thromboembolic risk (OR: 2.15, 95% CI: 2.08–2.24). Heterogeneity was moderate ($I^2 = 67.59\%$).

Conclusion: The meta-analysis confirms a two-fold increased CVT risk among OCP users. The systematic review and meta-analysis demonstrate a strong triangular correlation between religio-cultural practices, oral contraceptive use, and thromboembolic risk. Public health initiatives emphasize education, hydration, counselling, and safer menstrual management strategies.

Keywords: Cerebral venous thrombosis (CVT), Thromboembolic risk, Hormonal contraceptives (HCs), Religious practices, Cultural customs.

INTRODUCTION

Pregnancy and fertility are not diseases; they are natural physiological processes. However, classifying them as medical conditions allows certain entities to position contraception as a "cure"¹. Globally, 46% of 966 million reproductive-age women use short-acting contraceptives like condoms, OCPs, and injectables, while 44% rely on long-acting methods, and less than 10% use traditional methods. In 2020, 150 million (15.7%) women used OCPs². In India, modern contraceptive use is 47.8% (NFHS-IV)³, but only 3.1% of married women use OCPs⁴. In Tamil Nadu, OCP use is 0.7%⁵. Among contraceptive users aged 15–44, 25% choose OCPs, with combined hormonal pills being the most common⁶.

The link between COCs and venous thrombosis was first identified in 1961^{7,8}. Thrombotic risk factors include genetic predispositions such as factor V Leiden mutation, prothrombin G20210A mutation, and protein C/S deficiency, alongside acquired conditions like surgery, pregnancy, cancer, obesity, and hormonal therapy^{9,10}. Factor V Leiden disrupts activated protein C (APC) function, while TAFI stabilizes fibrin clots, increasing thrombosis risk^{10,11}. Estrogen in COCs amplifies coagulation by increasing procoagulant factors and reducing anticoagulants, leading to APC resistance¹². First-pass metabolism enhances coagulation, while levonorgestrel-

and desogestrel-containing COCs heighten prothrombotic effects. Hormonal and genetic factors together increase thrombotic risk, especially in thrombophilic individuals^{10,12}. Understanding these interactions aids in safer contraceptive choices. While primarily for contraception, 14% use OCPs for non-contraceptive benefits like menstrual regulation, pain relief, fibroids, endometriosis, migraines, and cultural or religious menstrual suppression^{13,14}.

The 2018 Supreme Court ruling overturning the Sabarimala temple's ban on menstruating women sparked protests, highlighting gender, religion, and politics. The Kerala government's Women's Wall and the entry of two women symbolized resistance to menstrual stigma. Across religions, menstrual restrictions persist, often labeling menstruating individuals as ritually impure. While some communities adhere strictly to these traditions, others challenge them for inclusivity. In Kerala, Christian and Hindu communities follow varied menstrual norms, with some practicing purification rituals and others rejecting them. Myths in Hindu traditions associate menstruation with supernatural consequences, reinforcing stigma and exclusion. Legal battles and activism continue to push for societal change in religious and cultural spaces^{15,16}.



Cultural restrictions also impact education. A study in rural Ghana found 85.7% of girls were barred from religious activities, 73.2% were deemed impure, and 36.4% were discouraged from discussing menstruation. Schools lacked hygiene facilities, leaving many unprepared for menarche. Younger girls (10–14 years) had significantly lower menstrual knowledge (aOR 0.20, 95% CI 0.08–0.48), and those without TV or radio access were 2.42 times more likely to be unaware (95% CI 1.41–4.15). The study underscores the need for menstrual education to challenge restrictive norms¹⁷.

Due to these restrictions, many use oral contraceptives (OCs) for menstrual suppression despite thromboembolic risks. A Study suggest it offers safe short- and long-term benefits, especially for adolescents with disabilities. Many prefer fewer periods for convenience in academics, sports, or personal reasons¹⁸. As this approach gains popularity, healthcare providers play a vital role in educating individuals on menstrual suppression's safety and potential risks. Research and reporting on OC use for religious purposes in India remain lacking. Unregulated OTC access and societal pressure contribute to misuse, raising concerns about thromboembolic risks. The increasing use of OCs for religio-cultural reasons underscores the urgent need for awareness, regulation, and further research to ensure safer contraceptive practices and informed decision-making.

1 METHODOLOGY

This systematic review and meta-analysis were conducted in accordance with a predetermined protocol aligned with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review encompasses literatures published up to 2024 and includes a comprehensive search strategy, data collection, and analysis.

1.1 Objectives

1. To provide awareness and education to women on contraceptive use for religious purpose and its Cerebral venous thrombosis risk.
2. To determine the association between oral contraceptive use and an increased risk of thromboembolic events.

1.2 Literature Search

The primary sources for the systematic review included reputable databases such as PubMed, Science direct and Google scholar. Additionally, supplementary hand searches and cross-referencing were performed to ensure a thorough exploration of the literature.

1.2.1 Search Methodology:

- The search utilized both free-text and medical subject headings to capture relevant literature.
- Focused solely on articles and documents published in the English language.

1.2.2 Research Themes

The search was organized around three key themes:

a) Exposure-related Terms:

Terms included "Oral Contraceptive", "Hormonal Contraceptives", "COC" and "OC pills."

b) Reasons for Use:

Included terms such as "Cultural customs" and "Religious."

c) Outcomes:

Concentrated on "CVT", "Central Venous Thrombosis" and "Thromboembolic."

The terms from the three themes were combined using the Boolean operator "AND" to refine and enhance the search results.

1.2.3 Manual Search

A manual search was conducted for studies up to 2024, and reference lists were reviewed to identify relevant but potentially overlooked or uncited articles.

1.3 Selection criteria

1.3.1 Inclusion Criteria:

- a) The review incorporated a diverse range of study designs, encompassing: Case reports, Case Series, Case-control studies, Reviews of case reports, Prospective studies, Retrospective studies, Longitudinal studies and Cohort studies.
- b) The studies focusing on patients who takes oral contraceptives for cultural and religious purpose and also other reasons.
- c) The study population was limited to women of reproductive age, specifically 19–60 years of age.

1.3.2 Exclusion Criteria:

- a) The studies involving male patients.
- b) Other language studies except English.
- c) Studies were excluded if the study population included pregnant women or post-partum women.

1.4 Data Extraction

This study systematically extracted data from eligible studies using a standardized form. It aims to evaluate the risk of cerebral venous thrombosis (CVT) in women using oral contraceptives (OCs), particularly those delaying menstruation for religious reasons. To provide a broader context, studies on OC use for other purposes were also included. The meta-analysis focuses on quantifying the association between contraceptive use and thromboembolic event risk, selecting studies that directly assess this relationship.



1.5 Quality assessment

For the systematic review, study quality was assessed using the JBI appraisal checklists for case report ¹⁹, case series ²⁰, cross-sectional ¹⁹ and cohort studies ¹⁹, with studies appraised as Include, Exclude and Seek further info. For the meta-analysis, the Newcastle–Ottawa Scale (NOS) ²¹ was used, applying the case-control and cohort study forms (maximum 9 points: selection (4), comparability (2), exposure/outcome (3)). Any discrepancies were resolved through discussion with a third author. The results of the analysis were presented in a narrative format to facilitate clarity and comprehensibility.

1.6 Data Synthesis and Analysis

This meta-analysis will include eligible studies, extract data systematically, and use a random-effects model to estimate the pooled odds ratio for thromboembolic risk Heterogeneity will be assessed using the I² statistic, and a forest plot will be used to visualize effect sizes in Advanced Excel.

2 RESULTS

Cerebral venous thrombosis (CVT) is increasingly recognized as a significant health concern, particularly in women who use oral contraceptive pills (OCPs) for non-contraceptive indications. Women using oral contraceptives (OCPs) to delay menstruation during religious observances face an increased risk of cerebral venous thrombosis (CVT).

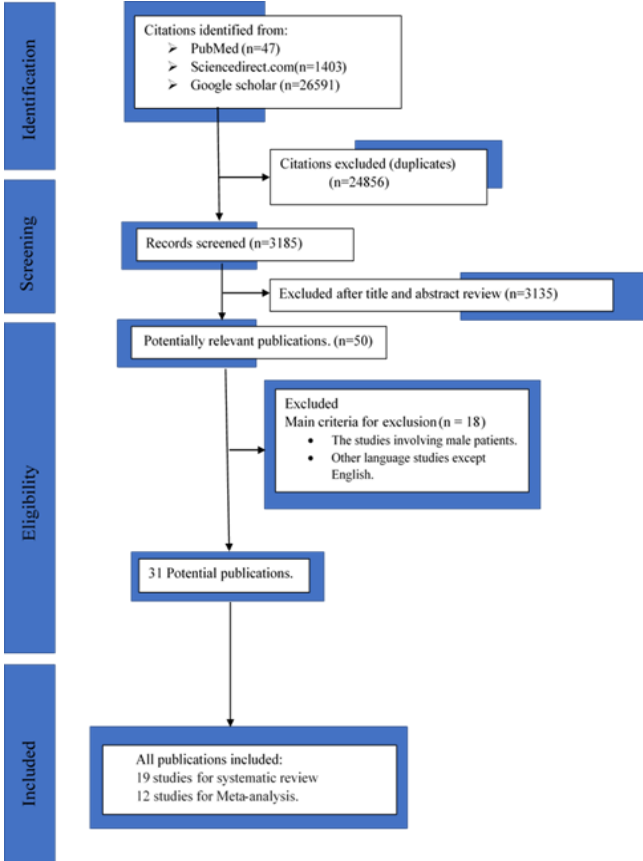


Figure 1: Flowchart illustrating the Selection Process of Studies included in Systematic Review and Meta-Analysis.

Table 1: Quality Assessment of the Meta-analysis.

Category	Case-Control Studies	Cohort Studies	Philip E. Sartwell et al. (1969)	Øjvind Lidegaard et al. (1993)	Øjvind Lidegaard and Svend Kreiner (1998)	Bloemenkamp et al. (1999)	Bloemenkamp et al. (2000)	Øjvind Lidegaard et al. (2002)	H.E. Seaman et al. (2003)	Øjvind Lidegaard et al. (2009)	Øjvind Lidegaard et al. (2011)	Saadatnia et al. (2012)	Emmanuelle Le Moigne et al. (2013)	Yana Vinogradova et al. (2015)
	Selection	Selection	★	★	★	★	★	★	★	★	★	★	★	★
Selection	1) Is the case definition adequate?	1) Representativeness of the exposed cohort	★	★	★	★	★	★	★	★	★	★	★	★
	2) Representativeness of the cases	2) Selection of the non-exposed cohort	★	★	★	★	★	★	★	★	★	★	★	★
	3) Selection of Controls	3) Ascertainment of exposure	★	★	★	★	★	★	★	★	★	★	★	★
Comparability	4) Definition of Controls	4) Demonstration that outcome of interest was not present at the start of study	★	★	★	★	★	★	★	★	★	★	★	★
	1) Comparability of cases and controls based on design or analysis	1) Comparability of cohorts based on design or analysis	★ ★	★ ★	★★	★ ★	★ ★	★ ★	★ ★	★ ★	★ ★	★ ★	★	★★
Exposure/Outcome	1) Ascertainment of exposure	1) Assessment of outcome	★	★	★	★	★	★	★	★	★	★	★	★
	2) Same method of ascertainment for cases and controls	2) Was follow-up long enough for outcomes to occur?	★	★	★	★	★	★	★	★	★	★	★	★
	3) Non-response rate	3) Adequacy of follow-up of cohorts	★	★	★	★	★	★	★	★	★	★	★	★
			9	9	9	9	9	9	9	9	9	9	8	9

Quality assessment of the systematic review included 19 studies, comprising 9 case reports (47.37%), 2 case series (10.53%), 1 cross-sectional study (5.26%), and 9 cohort studies (47.37%), all appraised as "include" using the JBI checklist. In the meta-analysis, 12 studies were assessed using the Newcastle-Ottawa Scale (NOS). Among the 9 case-control studies (75%), all scored 9 (100% high quality). Of the 3 cohort studies (25%), 2 scored 9 (66.67%), while one scored 8 (33.33%), resulting in an overall high methodological quality. The average NOS scores were 9 for case-control studies and 8.67 for cohort studies (Table 1).

This review examines CVST cases linked to oral contraceptive use for religious and other reasons. Prolonged and short-term OCP use, especially during fasting or postpartum dehydration, increases risk. CVST is associated with norethisterone in PCOS and hyperhomocysteinemia. Risk assessment is crucial for prevention, particularly in high-risk periods. The study characteristics of the systematic review are summarized in tabular format (Table 2,3).

Table 2: Characteristics of studies included for Systematic review.

Study number	Title of the study	Author(s)	Type of Study	Study Objective
1	Cerebral venous thrombosis in association with oral contraceptive use	VD Maheswari et al. (2004) ²²	Case Report	CVT in a woman using MALA-D oral contraceptive for polymenorrhea
2	Oral Contraceptives and Cerebral Venous Thrombosis: case report and a brief review of literature	Mughis Sheerani M. et al (2006) ²³	Case report	Evaluate probable vascular complications of short-term OCP consumption.
3	Central Venous Sinus Thrombosis in a Young Woman Taking Norethindrone Acetate for Dysfunctional Uterine Bleeding: Case Report and Review of Literature	Rajesh Rajput et al. (2008) ²⁴	Case Report	CVST following norethindrone acetate use for DUB due to PCOS
4	The relation between short-term oral contraceptive consumption and cerebrovascular, cardiovascular disorders in Iranian women attending Hajj	Azarpazhooh MR. et al (2008) ²⁵	Cohort study	Investigate the relationship between short-term OCP consumption and cerebrovascular/cardiovascular disorders in Iranian women attending Hajj.
5	The Relation between Short Course Oral Contraceptive Consumption and Cerebral Vein Thrombosis in Ramadan	Morteza Saidee. et al (2008) ²⁶	Prospective study	Investigate CVT incidence and its temporal relation to Ramadan in fasting women.
6	Oral Contraceptive Pills Consumption and Cerebral Venous Thrombosis	Kavian Ghandehari. et al (2009) ²⁷	Prospective observational study	Investigate CVT cases linked to OCP use during Ramadan/Hajj and emphasize public awareness.
7	Cerebral Venous-Sinus Thrombosis: A Case Series Analysis	Ashjazadeh N. et al (2011) ²⁸	Case series	Analyze CVT cases linked to OCP use, evaluate manifestations, radiological, and prognostic characteristics.
8	Cerebral vein thrombosis in women using short course oral contraceptive consumption	Sasannejad P. et al (2012) ²⁹	Cohort study	Study CVT incidence and its relation to Ramadan, highlighting short-term OCP use as a risk factor.
9	Incidence of Cerebral Venous Thrombosis in Iranian Women: A Longitudinal Two-Year Study in Zanjan Province of Iran	Ali Niksirat. et al (2014) ³⁰	Longitudinal descriptive study	Investigate the link between OCP use during Ramadan/Hajj and increased CVT risk.
10	Norethisterone induced cerebral venous sinus thrombosis (CVST): a rare case report and review of literature	Ramya T. et al. (2014) ³¹	Case Report	CVT linked to norethisterone in PCOS with hyperhomocysteinemia
11	Cerebral Venous-Sinus Thrombosis: Risk Factors, Clinical Report, and Outcome. A Prospective Study in the North East of Iran	Farzadfard MT. et al.(2015) ³²	Prospective study	To determine the demographic, clinical patterns, etiologies and prognostic factors of CVST in the North East of Iran.
12	A case-series study of cerebral venous thrombosis in women using short course oral contraceptive	Khomand P. et al (2016) ³³	Retrospective case series	Highlight the association between Ramadan, OCP use, and CVT risk among women.
13	Cerebral venous thrombosis following the use of oral contraceptive: A case report	Mehrafza Mir et al. (2016) ³⁴	Case Report	Diagnosis, management, and treatment of CVT in a young girl

14	Norethisterone enanthate-induced cerebral venous sinus thrombosis (CVST)	Mandreker Bahall et al. (2017) ³⁵	Case Report	CVST linked to long-term use of depot progesterone injections
15	Prognosis of fasting in patients with cerebral venous thrombosis using oral contraceptives	Masoud Ghiasian M. et al (2019) ³⁶	Cross-sectional study	Evaluate fasting's impact on CVT among OCP users in Ramadan.
16	Prevalence of cerebral venous thrombosis with the use of oral contraceptive pills during the Holy month of Ramadan	AlSheef M. et al (2020) ³⁷	Retrospective study	Identify the prevalence, clinical characteristics, risk factors, and management of CVT among fasting women using OCPs during Ramadan to enhance the standard of care for women's health.
17	Cerebral vein thrombosis in a woman using oral contraceptive pills for a short period of time: a case report	Somayeh Moeindarbari et al. (2022) ³⁸	Case Report	CVT in a patient with endometriosis and prolonged Diane-35 use
18	Norethisterone-induced Subacute on Chronic Cerebral Venous Sinus Thrombosis with Secondary Intracranial Hypertension in a Young Woman: A Case Report	Garikapati Kavitha et al. (2022) ³⁹	Case Report	CVST case in a young female after norethisterone use for AUB therapy
19	Cerebral venous sinus thrombosis due to desogestrel intake in a young lady: A case report	Deepak Sharma et al. (2024) ⁴⁰	Case Report	Case of CVST in a young woman with no apparent risk factors, later associated with desogestrel use for AUB and elevated homocysteine

Table 3: Characteristics of studies included for Systematic review.

Study number	Subject (Female)	Age	Signs and Symptoms	Drug	Duration	Reasons	Diagnosis	Complications
1	1 case	43	Sudden headache, vomiting, blurred vision, slurred speech, seizures	MALA-D (Levonorgestrel & Ethinyl Estradiol)	2 years	Polymenorrhea	CT scan MRI angiography MRI venography Central nervous system (CNS) examination Fundus examination	Thrombosis in left transverse/sigmoid sinuses
2	1 patient, a 42-year-old housewife.	42 years	Left-sided numbness, weakness, acute neurological deficits.	Oral contraceptive pills (OCPs).	Several days	Used OCPs to postpone menstruation for Hajj.	MRI revealed parietal stroke, while MRV demonstrated thrombus in the right transverse sinus.	Thrombus in right transverse sinus observed on MRV; parietal stroke.
3	1 case	23	Severe headache, vomiting, right-sided weakness, seizures	Norethindrone acetate (5 mg/day)	7 days	DUB secondary to PCOS	MRI MR venography Screening for thrombophilia (Protein C, Protein S, Antithrombin III) Antiphospholipid antibodies Factor V Leiden mutation Prothrombin gene mutation Serum homocysteine levels Methylenetetrahydrofolate reductase (MTHFR) mutation screening	Left frontal lobe infarction, Thrombosis in multiple sinuses
4	896 individuals with 642 completed follow-up.	<50 years	Migraine, transient hypertension, MI, vascular complications, papillary edema.	LD (35 µg ethinyl estradiol, 0.3 µg norgestrel); HD (50 µg ethinyl estradiol, 0.5 µg norgestrel).	29+ consecutive days	Stress, dehydration, and fasting rigors during Hajj may trigger vascular disorders.	Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) studies were used to confirm CVT.	Vitamin B12 deficiency

5	24 cases-19 females.	38 years	Headache, seizures, focal neurological deficits, dehydration, fasting fatigue.	LD and HD formulations.	1-2 months	OCPs used to postpone menstruation during Ramadan and Hajj.	Neuroimaging involved brain CT scans (with or without contrast), brain MRI, MR-Venography, temporal bone CT scan, and, in some cases, four-vessel brain angiography.	Predisposing factors like dehydration and fasting exacerbate vascular conditions.
6	51 females.	18-62 years	Dehydration during fasting, headache, and neurological deficits.	LD and HD formulations.	3 months	Religious practices during Ramadan/Hajj encourage short-term OCP use.	Diagnosis was based on MRI and MR Venography with a modified Rankin Scale (mRS) used to assess neurological outcomes.	Parenchymal hemorrhage, subarachnoid hemorrhage.
7	124 patients - 87 women.	34.01 ± 10.25	Headache, papilledema, seizures.	Oral contraceptive pills (OCPs).	>1 month	Used OCPs during Ramadan or Hajj to delay menstruation; CVT developed.	Cerebral MRI and magnetic resonance venography (MRV), contrast digital subtraction venography, brain and paranasal sinuses MRI, CT scans of the chest, abdomen, and pelvis, and bone scans	18 patients died; recurrent thrombosis (DVT, hepatic vein thrombosis); hemorrhage on CT scan associated with poor prognosis.
8	70 cases-59 females.	34 ± 7 years	Seizures, focal neurological deficits.	Short-course OCP (23 cases); long-course OCP (8 cases).	≥1 month	OCP use to postpone menstruation during Ramadan fasting.	CVT diagnosis was confirmed through clinical presentations and neuroimaging findings.	Ischemic venous infarct, parenchymal hemorrhage, subarachnoid hemorrhage.
9	26 patients	37.6 ± 10.21 years	Dehydration combined with OCP use as a risk factor.	Various contraceptive formulations, including LD, cyproterone, DMPA.	<1 month to >1 month	Religious motivation to delay menstruation using OCPs.	Lab work for CVT included CBC, FANA, ANCA (P and C), Anti ds DNA, Pro-C, Pro-S, Antithrombin, APCR, Hyperhomocysteinemia, APL-Ab, ACL-Ab, Lupus Anticoagulant, β-2 Glycoprotein, and Prothrombin G20210A Mutation.	Stevens-Johnson syndrome, hemorrhagic infarction, diabetic ketoacidosis.
10	1 case	24	Headache, vomiting, focal seizures, irregular menstrual cycles	Norethisterone (5 mg TDS)	50 days	PCOS, irregular bleeding	MRI MR venography CT scan (follow-up) Thrombophilia profile (ANA, anti-PLP antibodies, Factor V Leiden mutation) Serum homocysteine levels Ultrasound for polycystic ovaries	Frontal lobe hemorrhages and dural venous thrombosis
11	Sixty patients-86.7% women(52)	38.11± 11.30 years	Increased intracranial pressure. The most frequent clinical manifestations were headache in 60 (100%), papilledema in 51 (85%), seizure in 30 (50%), hemiparesis in 17 (28.3%), and decreased level of consciousness in 27	Oral Contraceptive Pills (OCPs)	shorter than three months	Religious ceremony such as Hajj or Ramadan fasting, and developed CVST during the period of the drug consumption.	Cerebral magnetic resonance imaging (MRI) and magnetic resonance venography (MRV), along with brain and paranasal sinuses MRI, were performed. Plasma concentrations of proteins C, S, antithrombin III, and antibodies like anticardiolipin, antinuclear, anti-double-stranded DNA, and hypercoagulability tests were also measured.	Hypercoagulability worsens after delivery because of dehydration and trauma



			patients (45%).					
12	9 patients.	25-49 years	Headache, papilledema, seizures, blurred vision, vomiting, neurological deficits, hemorrhage.	LD: Ethinyl estradiol 0.03 mg + levonorgestrel 0.15 mg.	>1 month	Fasting during Ramadan with prolonged OCP use to delay menstruation.	CVT diagnosis was based on clinical signs. MRV. Paraclinical assessments for thrombophilia were conducted, including tests for protein C and S, antiphospholipid antibodies, and vasculitis markers such as antinuclear antibody and anti-double stranded DNA (dsDNA).	Superior sagittal sinus, bilateral cortical, transverse sinus thrombosis extending to jugular vein.
13	1 case	17	Severe headaches, nausea, vomiting, double vision	Combined oral contraceptive pills	10 days	PCOS, menometrorrhagia	CT scan MR venography Complete blood count (CBC) Lupus anticoagulants (LA) Protein C and S AntidsDNA Antiphospholipid antibodies Anticardiolipin antibodies c-ANCA (Anti-PR3) and P-ANCA Factor V Leiden SGPT and SGOT	Sagittal sinus thrombosis
14	1 case	23	Mild headache worsening over days, vomiting, syncope	Norethisterone enanthate (depot injection)	2 years	Long-term contraception	CT scan MRI MR venography	Sinus thrombosis in the superior sagittal, right transverse, and sigmoid sinuses
15	58 patients.	38.91 ± 8.39 years	Higher incidence of focal neurological deficit and hemorrhage among fasting women on OCPs.	Oral contraceptives (OCPs).	6-12 months	Higher CVT risk during Ramadan due to OCP use and fasting.	Diagnosis was based on MRI and MR Venography with a modified Rankin Scale (mRS) used to assess neurological outcomes.	None reported.
16	108 female patients with CVT (39 due to OCP use)	30-50 years	Headache, seizure, vomiting, blurred vision, impaired consciousness, weakness, numbness, confusion, abdominal pain, fever, dizziness, neurological deficit, and others.	Third-generation OCP based on estradiol component.	1 month and more	Women use OCPs to postpone menstruation for religious practices during Ramadan or Hajj.	Diagnosis of CVT typically involved the use of CT or magnetic resonance imaging (MRI), and magnetic resonance angiography (MRA).	Risk factors include prothrombin gene mutation, protein C/S deficiency, dehydration, family history, lupus; management with anticoagulation therapy.
17	1 case	31	Headache, fatigue, low-grade fever, chickenpox lesions	Diane-35 (cyproterone & ethinyl estradiol)	3 months continuous use	Post-endometriosis surgery	CT scan MR venography	Vein occlusion in the right sinus
18	1 case	22	Worsening headaches, projectile vomiting, mild tachycardia	Norethisterone acetate (10 mg OD)	5 days of therapy	PCOD, continuous bleeding	MRI Angiography	Thrombosis in superior sagittal sinus and right transverse sinus
19	1 case	25	Unconscious, severe diffuse headache, vomiting, seizures, altered sensorium	Desogestrel (150 µg/day)	Started 2 months back	AUB	Liver and renal function tests Electrocardiogram (ECG) Serum electrolytes Chest X-ray CT scan MRI Cerebrospinal fluid (CSF) analysis Viral encephalitis testing	Thrombosis in the superior sagittal sinus and hemorrhagic transformation

Table 4: Study characteristics of included studies with OC use for religious reasons.

Characteristics	No. of studies	No. of patients
Total	12	1072
Age (Mean age)	12	32.72 ± 7.71 years
Oral contraceptives		
OCPs (Specific drug not reported)	5	222
Third generation OCP(COC)	1	39
LD Ethinyl estradiol and Norgestrel(COC)	1	9
LD Ethinyl estradiol and Norgestrel + HD Ethinyl estradiol and Norgestrel (COC)	3	712
Cyproterone compound (COC)	1	64
LD(COC) + Cyproterone compound(COC) + Depot medroxyprogesterone acetate (POC)	1	26
Diagnostic tool		
CT and MRA	2	63
MRI and MRV	3	694
CT, MRI and MRV	2	83
CT, MRI, MRV and plasma concentrations	2	139
MRV and plasma concentrations	1	9
MRI, MRV and mRS	1	58
Plasma concentrations	1	26
Study type		
Retrospective study	3	135
Prospective study	3	122
Longitudinal study	1	26
Cross-sectional study	1	58
Cohort study	2	666
Case report	1	1
Case control study	1	64
Publication year		
2006 to 2011	5	800
2012 to 2020	7	272
Reasons for intake		
Religious reasons to postpone menstruation	12	1072
Duration of OCP intake		
Study Number	≤ 3 months	> 3 months
Mughis Sheerani M. et al (2006)	NR*	
Azarpazhooh MR. et al (2008)	Yes	-
Morteza Saidee. et al (2008)	Yes	
Kavian Ghandehari. et al (2009)	-	Yes
Ashjzadeh N. et al (2011)	Yes	-
Sasannejad P. et al (2012)	Yes	-
Saadatnia M. et al (2012)	-	Yes
Ali Niksirat. et al (2014)	-	Yes
Farzadfard MT. et al. (2015)	Yes	-
Khomand P. et al (2016)	Yes	-
Masoud Ghiasian M. et al (2019)	-	Yes
AlSheef M. et al (2020)	Yes	-

*NR- Not reported

The systematic review included 1,072 patients, mostly middle-aged women (mean age 32.72 ± 7.71 years), using oral contraceptives (OCPs) for religious reasons. Combined low-dose and high-dose ethinyl estradiol with levonorgestrel-based OCPs were the most studied, while

other regimens were less explored. MRI and MRV were the preferred diagnostic tools, but diagnostic practices varied, with limited use of multi-modal approaches. Most studies were observational, with few prospective or case-control studies to establish stronger causal links.



Research increased after 2012, reflecting growing awareness, but societal pressure to postpone menstruation for religious reasons emerged as a significant issue driving OCP use, highlighting the need for broader discussion and alternatives to address such challenges.

Studies have investigated the duration of oral contraceptive pill (OCP) intake in relation to health outcomes. Overall, short-term OCP use has been more frequently investigated compared to long-term use. (Table 4 and Fig. 2).

The meta-analysis highlights a consistent association between oral contraceptive use and an increased risk of thromboembolic events. Most studies report significant odds ratios, with variations based on contraceptive type, hormonal composition, and duration of use. These results emphasize the need for individualized contraceptive counselling, especially for women with additional risk factors (Table 5).

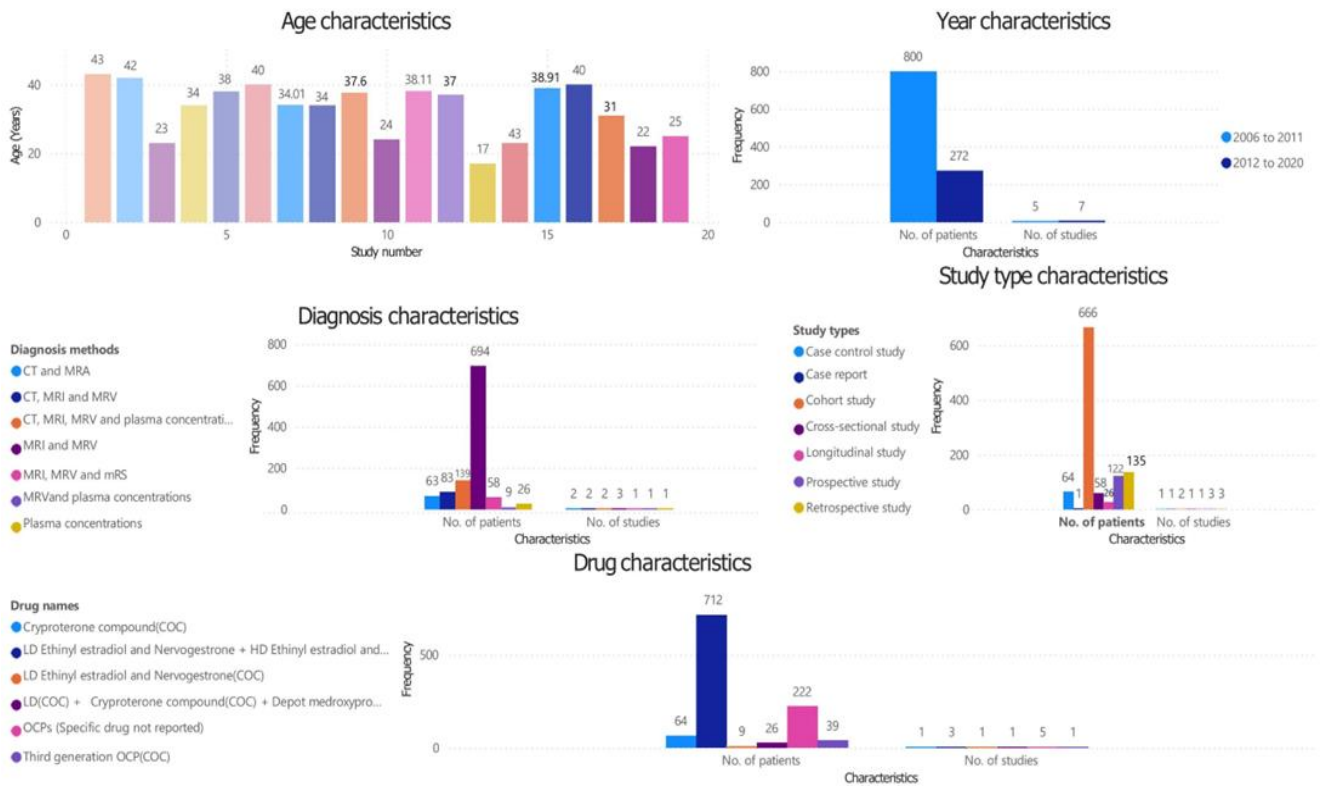


Figure 2: Visual representation of study characteristics of included studies with OC use for religious reasons.

Table 5: Meta-Analytical Assessment of Oral Contraceptive Use and Thromboembolic Risk

S.No	Study	Year	Study Design	Sample Size (Cases/ Controls)	Exposure	Outcome	Odds Ratio (OR)	95% Confidence Interval (CI)
1	Philip E. Sartwell et al. ⁴¹	1969	Retrospective case-control	175 / 175	OC use within 1 month before hospitalization	Idiopathic Thromboembolism	4.4	2.6 to 7.4.
2	Øjvind Lidegaard et al. ⁴²	1993	Retrospective case-control	320/ 1197	Oral contraceptive use	Cerebral thromboembolic attack	2.99	2.27 to 3.94
3	Øjvind Lidegaard and Svend Kreiner ⁴³	1998	Case-Control	219 / 1041	Oral contraceptive (OC) use (by generation, estrogen dose, and progestin type)	Cerebral thromboembolic attack (CTA)	2	1.44 to 2.78
4	Bloemenkamp et al. ⁴⁴	1999	Case-control study	185/ 591	Current oral contraceptive (OC) use,	First episode of venous thrombosis (deep	3.23	2.29, 4.54

					stratified by progestogen type and estrogen dose	vein thrombosis of the legs)		
5	Bloemenkamp et al. ⁴⁵	2000	Population- based case- control study (Leiden Thrombophilia Study)	109 / 65	Use of combined oral contraceptives (COCs), stratified by duration (≤6 months, 7–12 months, ≥13 months)	First episode of objectively confirmed deep vein thrombosis (DVT)	3.79	2.39 to 6.03
6	Øjvind Lidegaard et al. ⁴⁶	2002	Case-control	987 / 4054	Oral contraceptive use	First-time VTE	2.25	1.82 to 2.77
7	H.E. Seaman et al. ⁴⁷	2003	Cohort and nested case- control	179 / 1076	Cyproterone acetate with ethinyl estradiol (CPA/EE)	Risk of VTE	3.72	2.17 to 6.37
8	Øjvind Lidegaard et al. ⁴⁸	2009	National cohort	4213/10,443,160	Different hormonal contraceptive regimens	First-time VTE	2.03	1.91 to 2.16
9	Øjvind Lidegaard et al. ⁴⁹	2011	National historical registry cohort	4307/8,005,983	Combined oral contraceptives with different progestogens	First-time VTE	2.19	1.74 to 2.750
10	Saadatnia et al. ⁵⁰	2012	Case-control	64 / 232	OC use as Self- treatment, delaying menstruation for religious customs or traveling.	CVST	2.36	1.33 to 4.18
11	Emmanuelle Le Moigne et al. ⁵¹	2013	Prospective cohort	180 / 61	COC use during first VTE	Recurrence of VTE	0.9	0.32–2.73
12	Yana Vinogradova et al. ⁵²	2015	Nested Case- Control Study	10,562 / 42,034	Combined Oral Contraceptives (various progestogens)	Venous Thromboembolism (VTE)	2.16	2.05–2.27

In the present meta-analysis, twelve studies were included in the meta-analysis based on the availability of requisite data. The findings from this meta-analysis indicate a significant association between hormonal contraceptive use and an increased risk of thromboembolic events. The pooled odds ratio (OR) from the random-effects model is 2.15 (95% CI: 2.08–2.24), suggesting that women using hormonal contraceptives have more than twice the risk of developing thromboembolic events compared to non-users.

Heterogeneity in the included studies was moderate ($I^2 = 67.59\%$), indicating some variability in effect sizes across studies. Differences in study design, population characteristics, and contraceptive formulations likely contribute to this heterogeneity. One study reported no significant association, which may be due to confounding factors such as genetic predisposition, lifestyle variables, or concurrent medical conditions. However, the overall trend

across studies consistently demonstrates an elevated risk (Fig. 3).

3 DISCUSSION

The review analyzed 1,072 patients (mean age 35.56 ± 8.50 years) using OCPs for religious reasons, with ethinyl estradiol and levonorgestrel being the most studied. MRI/MRV were primary diagnostic tools. Observational studies dominate, emphasizing the need for large-scale research on risk factors and prevention. Societal pressure to delay menstruation is a key factor, highlighting the need for large-scale studies on long-term risks and prevention.

The findings from our meta-analysis, indicating a pooled odds ratio (OR) of 2.15 (95% CI: 2.08–2.24) for thromboembolic events among hormonal contraceptive users, align with and add to the existing evidence from prior studies. For instance, one study reported that combined oral contraceptive (COC) use increased venous thrombosis



risk by 3.5 times (95% CI: 2.9–4.3) compared to non-users, with higher risks observed for contraceptives containing gestodene, desogestrel, cyproterone acetate, or drospirenone⁵³. Another study highlighted that oral contraceptives with levonorgestrel increased VT risk by 2.79–4.07, while non-oral contraceptive methods like vaginal rings and patches presented even higher risks (ORs of 6.5 and 7.9, respectively)⁵⁴. A meta-analysis further

supported these findings, reporting an overall OR of 3.41 (95% CI: 2.98–3.92) for OC users, with variations based on contraceptive type and presence of genetic mutations⁵⁵. Interestingly, while oral progestin-only contraceptives (POCs) did not show an increased thromboembolism risk (OR 1.06, 95% CI: 0.70–1.62), injectable POCs were associated with higher risk (OR 2.62, 95% CI: 1.74–3.94)⁵⁶.

Forest plot depicting thromboembolic risk associated with contraceptive use.

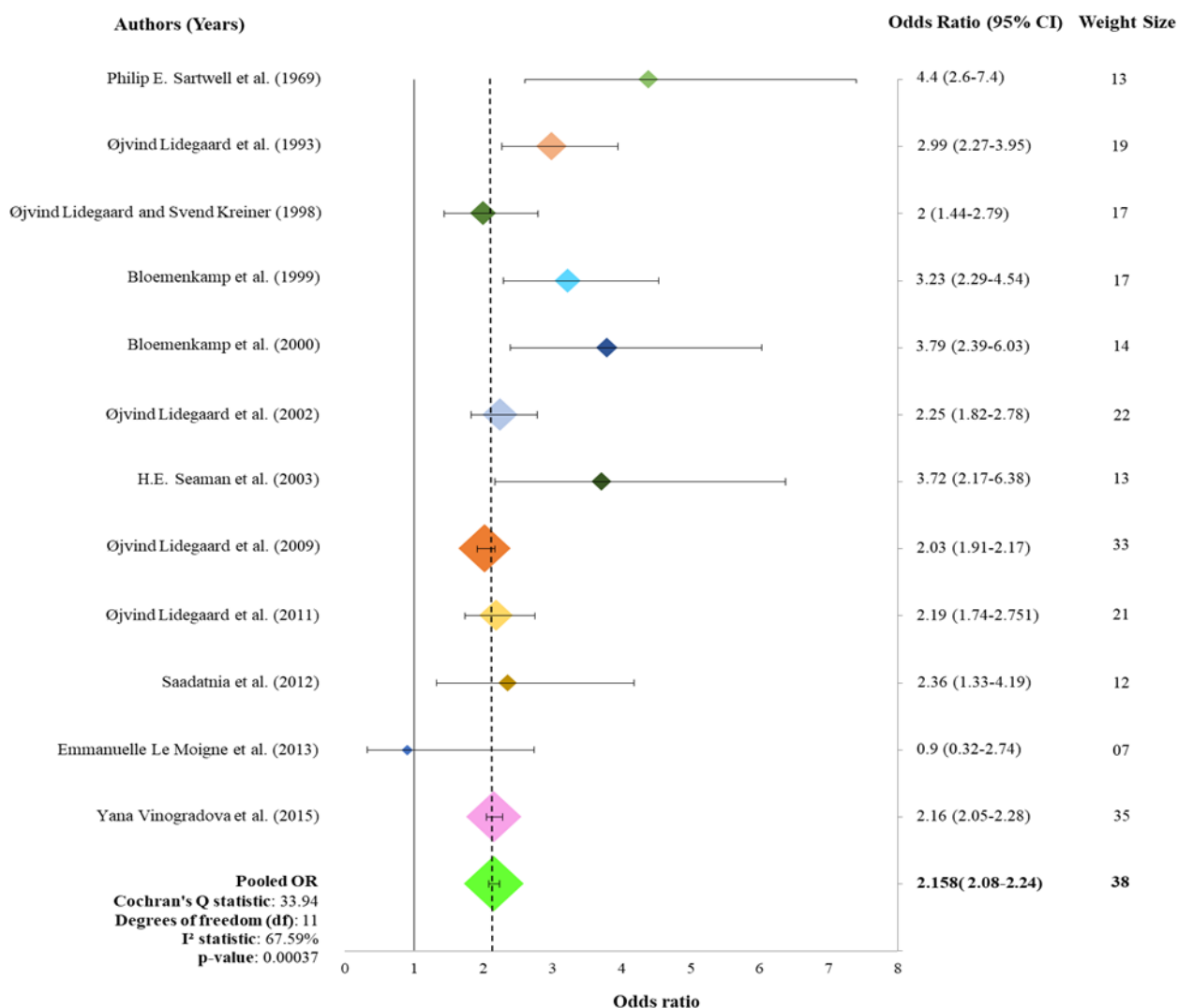


Figure 3: Forest Plot Depicting the Odds Ratios for the Association Between Oral Contraceptive Use and Thromboembolic Risk

Although OCP use alone is a significant risk factor, it is important to consider the interplay of additional risk factors that may exacerbate the risk of CVT. Genetic predispositions, such as factor V Leiden mutation and prothrombin gene mutations, significantly amplify the thrombotic risk in OCP users⁵⁷. Studies have shown that women with factor V Leiden mutations who use OCPs have an exponentially increased risk of venous thromboembolism compared to those without these

mutations⁵⁸. Furthermore, acquired risk factors such as dehydration, fasting, and prolonged immobility can further contribute to a prothrombotic state, increasing the likelihood of CVT in OCP users⁵⁹.

From a public health perspective, increasing awareness about the risks of OCP-associated thrombosis is essential. Although OCPs remain a widely used and effective method of contraception, patients should be informed about alternative contraceptive options⁶⁰.

Women should exercise caution when using oral contraceptives (OCs), especially for non-medical purposes like postponing menstruation for religious reasons ⁶¹. Prolonged or unnecessary use may increase the risk of thromboembolic events, particularly in those with risk factors such as smoking, obesity, thrombophilia, or migraines with aura ⁶². Safer alternatives, including progestin-only pills, intrauterine devices (IUDs), or non-hormonal methods, should be considered ⁶³. It is essential to consult healthcare professionals to assess individual risk and make informed choices regarding contraceptive use.

It is important to highlight that our systematic review included studies focusing on OCP use for delaying menstrual cycles for religious purposes, recognizing the cultural relevance of this practice. However, the meta-analysis specifically included studies related to OCP use and thromboembolic events, regardless of the reason for OCP intake. This distinction is crucial, as it underscores the need to consider different contexts and motivations for OCP use when interpreting the results.

This study has limitations, including heterogeneity among studies due to differences in design, population, and OCP formulations, making definitive conclusions challenging. Residual confounding cannot be ruled out.

Research on OCP use for cultural or religious reasons could offer deeper insights into unique risk profiles. Public health initiatives, including education on OCP risks during fasting, can empower women to make informed decisions. Healthcare providers should counsel on safer practices, hydration, and alternative menstrual management. For those with genetic risks, thrombophilia testing and personalized contraceptive advice are crucial. Collaborative efforts can help reduce CVT risk and improve health outcomes.

4 CONCLUSION

This meta-analysis confirms a significant association between oral contraceptive pill (OCP) use and an increased risk of cerebral venous thrombosis (CVT), demonstrating a two-fold elevated risk among OCP users. Although the systematic review included studies where OCPs were used to delay menstruation for religious purposes, the meta-analysis focused on thromboembolic events irrespective of the reason for OCP intake. Further research is needed to explore safer contraceptive alternatives and to enhance understanding of the underlying mechanisms linking OCP use to thromboembolic events.

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