

# Systematic Review: Correlation Between Hormonal Contraception with Spheno-Orbital Meningioma

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**Abstract— Background:** Spheno-orbital meningioma (SOM) is a rare tumor of the meningioma that arises from the sphenoid that can have a periorbital extension. This tumor contributes for 2-9% of the intracranial meningiomas. Arising from the sphenoid wing, SOM consists of two components such as an intraosseous growth with secondary associated hyperostosis. Risk factors for this tumor include hormones and gene mutation. This study seeks to examine the relation between hormonal contraception and spheno-orbital meningioma. **Methods:** A literature search was conducted from four databases, which are Scopus, Science Direct, PubMed, and Google Scholar. The articles are searched using the Boolean logic of keywords. Through these, 303 research articles were found (ScienceDirect = 200, Scopus = 78, Pubmed = 10, Google Scholar = 15). These articles are then screened and 4 articles are determined to be used in this review. **Results:** The studies included for this review stated that most of SOM patients are female. They also reported hormonal contraception usage on these patients. Progesterone analogs dominate the therapy used. **Conclusions:** The type of hormonal contraception is linked with SOM, as can be seen from the many incidences coming from a certain hormonal contraception. However, the correlation between hormonal contraception and the location is yet to be studied.

**Keywords—** Meningioma, Spheno-orbital, Hormones, Contraception, Gene Mutation, Systematic Review

## I. INTRODUCTION

Meningiomas are derived from the meningotheial cells of the arachnoid mater. It is commonly arising in intracranial, intraspinal, or orbital locations, which includes the cerebral convexities that could associated with the falx cerebri or venous sinuses, olfactory grooves, sphenoid ridges, parasellar/suprasellar regions, optic nerves sheath, petrous ridges, tentorium, and posterior fossa. Spheno-orbital meningioma (SOM) is a rare tumor of the meningioma that arises from the sphenoid that can have a periorbital extension [1].

This tumor contributes for 2-9% of the intracranial meningiomas. Arising from the sphenoid wing, SOM consists of two components such as an intraosseous growth with secondary associated hyperostosis. This hyperostosis is able to spread to the sphenoid wing, orbital roof, superior orbital fissure, optic canal, and anterior clinoid process. Dural invasions are also often seen extends to said locations. SOMs are able to invade soft tissues around the temporal or the infratemporal muscles. Despite the invasive features, in most practical terms SOMs are benign [2].

The clinical manifestation of SOMs are based on the features of the tumor. The hyperostosis and dural invasions are the cause of proptosis as the most common presenting manifestation, followed by visual impairment which is caused by the invasion to optic canal and compression of the optic nerve, and ocular paresis. This is usually referred as the classic triad of SOMs. A CT Scan or MRI can be performed to determine if a case is a case of SOM [2].

Both external and internal exposure to hormones have been recognized as possible contributors to the onset of spheno-orbital meningiomas. Notably, research has highlighted connections between the utilization of hormonal contraception and the likelihood of developing these tumors. The utilization of hormonal contraception, particularly treatments involving progesterone, has been associated with a heightened likelihood of spheno-orbital meningiomas. This correlation is believed to stem from the hormonal effects on the growth and progression of these tumors, which are more prevalent among women [3].

## II. METHODS

### A. Study Selection

This review obtained studies from four databases, which are Scopus, Science Direct, PubMed, and Google Scholar. The articles are searched using the *Boolean logic* of keywords specified in the inclusion criteria. The studies are then filtered using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart, by filtering studies based on the relevance of keywords, abstract, and the content of the study.

### B. Inclusion and Exclusion Criteria

Included criteria for this review are: (1) cohort studies, (2) studies including female patients suffering from SOM, (3) female patients were on any hormonal contraceptions. The excluded criteria for this review are: (1) studies that are not discussing SOM, (2) Female patients not suffering from SOM, (3) Female SOM patients not having history of hormonal contraception usage, (4) studies published outside the range of 2014 – 2025.

### C. Data Extraction

Extracted data from each selected study including the type of hormonal contraception, the number of patients for each mentioned hormonal contraception, and the general information of the studies, such as the authors, publication

date, and additional information regarding the topic that is being studied.

III. RESULTS AND DISCUSSION

A. Characteristics of Selected Studies

303 research articles were found (ScienceDirect = 200, Scopus = 78, Pubmed = 10, Google Scholar = 15). These articles are then screened and 4 articles are determined to be used in this review. All of the included papers discussed about SOM patients with history of hormonal contraception usage. However, only 1 paper did not mention the specific type of hormonal contraception.

B. Demographics of Patients

All studies have one thing in common, which is the majority of patients suffering from SOM are women. 78/82 patients are female reported by [4], 119/130 female patients reported by [5], and both [6] and [7] reported all female patients with 20 and 3 patients reported respectively. This information is in line with other studies that reported majority of SOM patients are female, as can be seen from the Table I

TABLE I. Incidence of Spheno-orbital meningioma past 10 years studies

Literature	Country	Total SOM Patients	Male Patients	Female Patients
Young, <i>et al.</i> , 2019	England	24	2	22
Jiranukool, <i>et al.</i> , 2016	Thailand	26	1	25
Freeman, <i>et al.</i> , 2017	USA	25	2	23
Maschke, <i>et al.</i> , 2019	Austria	31	4	27

TABLE II. Number of Patients for Each Type of Hormonal Contraceptions

	Apra, <i>et al.</i> , 2020	Planty-Bonjour, <i>et al.</i> , 2024	Terrier, <i>et al.</i> , 2018	AbiJaoude, <i>et al.</i> , 2021	Total
Nomegestrol acetate		8/20		2/3	10/23(43.47%)
Chlormadinone acetate		2/20			2/20(10%)
Cyproterone acetate		2/20	5/119		7/139(5.03%)
Progesterone and nafarelin combined		1/20			1/20(5%)
Promegetone				1/3	1/3(33.33%)
Unspecified Progesterone Analogs	41/78				41/78(52.56%)
Unspecified oestrogenic treatment	13/78				13/78(16.67%)
Unspecified Menopausal Therapy	7/78				7/78(8.97%)

Studies has increasingly clarified the profound relationship between progesterone and spheno-orbital meningiomas (SOM). These tumors, which originate at the junction of the skull base and the orbit, are characterized by a remarkable sensitivity to sex hormones, particularly synthetic progestogens found in high-dose contraceptives and hormone replacement therapies. Research indicates that the sphenoid wing area is a primary site for "hormone-induced" meningiomas because the tumor tissue in this region frequently expresses progesterone receptors (PR) at higher densities than in other intracranial locations [11] [12]

A landmark national case-control study published, identified that certain synthetic progestogens significantly increase the risk of intracranial meningiomas [12]. The study found that prolonged use (over one year) of injectable medroxyprogesterone acetate (Depo-Provera) was associated

While the studies mentioned on the table did not report any history of hormonal contraception usage, there is an interesting similarity with the studies reviewed, that is the majority of studies reported have mean and median age of SOMs diagnosis at somewhere around 50 years of age.

Spheno-orbital meningiomas exhibit a distinct correlation with age, primarily manifesting as a disease of middle adulthood. The peak incidence typically occurs between the fourth and sixth decades of life, as stated before from the studies that the mean and median age of diagnosis in the 40s [8]. This age-related distribution is heavily influenced by hormonal factors; the high prevalence in middle-aged women suggests that the tumor's progression maybe linked to hormonal shifts occurring during or just before menopause.

C. Type of Hormonal Contraceptions

All of the studies mentioned in this review reported usage of hormonal therapy in patients. Progesterone analogs dominate the therapy used. The reported history of hormonal contraception for each study can be seen from the TABLE II.

All specified and unspecified hormonal contraception reveal that progestins to be the most common contraception seen in SOM patients. Supported by other studies such as, 96/101(95.04%) meningioma patients have a history of contraception usage with 95/96(98.95%) patients reported of receiving hormonal contraception [9]. [10] also reported similar finding of majority of meningioma patients (72/99(72.7%)) have a history of hormonal contraception usage.

with a 5.55-fold increased risk. This risk was even more pronounced for high-dose progestogens like cyproterone acetate (19.2-fold risk) and nomegestrol acetate (4.9-fold risk) [13]. Crucially, these hormone-associated tumors show a strong predilection for the skull base, which includes the spheno-orbital region [14].

D. Progesterone Receptors in Spheno-orbital Meningioma

Progesterone receptors are reported by [6], with it being present in 10/11(91%) patients, with high expression ranging from 70 – 100%. This report aligns with other studies that report progesterone receptors are more commonly found in meningioma. [15], reported positive progesterone receptors in 56/79(71%) patients, with mean progesterone receptors index of 21.4±2.8% and range between 0 - 79%. [16], reported progesterone receptors in 53/54(98.1%) meningioma patients.

Out of 48/53(90.6%) patients with positive progesterone receptors have a history of using hormonal contraceptives. The authors also reported 30/54(55.6%) patient's meningioma are located in sphenoid-orbital location.

Histopathological research indicates that the sphenoid-orbital region is a biological "hotspot" for hormone-sensitive tumors. Studies have confirmed that meningiomas of the skull base, particularly the sphenoid wing, exhibit a significantly higher density of progesterone receptors (PR) than those located on the brain's convexity. While general meningiomas show PR-positivity in roughly 70–80% of cases, sphenoid-orbital variants frequently reach 95% to 100% positivity [11].

The high concentration of PR makes these tumors uniquely reactive to exogenous progestogens found in contraceptives and hormone replacement therapies. When these receptors are activated by synthetic hormones like cyproterone acetate or medroxyprogesterone, they trigger a cascade that promotes not only the growth of the soft tumor mass but also hyperostosis (bone thickening). In the sphenoid-orbital region, this causes the sphenoid bone to expand into the orbital cavity, leading to the characteristic "bulging eye" (proptosis) and compression of the optic nerve [12].

#### IV. CONCLUSION

Sphenoid-orbital meningioma is affected by external hormone exposure; hormonal contraceptions in this case. The hormone that is heavily correlated with sphenoid-orbital meningioma is progesterone, thus hormonal contraceptions of the progestins are correlated. This is due to sphenoid-orbital meningioma arises from the sphenoid wing in which progesterone receptors density is markedly greater in these specific regions compared to the areas situated on the brain's convexity.

The hormones activated the receptors which promotes the growth of the tumor and also bone thickening which is considered to be the characteristic of this tumor. However, studies revealed that increased risk of sphenoid-orbital meningioma is found due to prolonged exposure of the hormonal contraception.

The author suggests future studies to discuss more about specific types of hormonal contraception, duration of usage, and the expression of progesterone receptors to provide additional information regarding the correlation between the topics.

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