Investigating the Clinical Implications and Prevalence of Distributive Frequency of Secretor and Non-Secretor Status of ABH Antigenic Substances as a Novel Risk Factor in Ectopic Pregnancy: A Systematic Review and Meta-Analysis of the Allele-Type Analysis from Published Studies.

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DOI: https://doi.org/10.51584/IJRIAS.2025.10040044

Received: 28 March 2025; Accepted: 03 April 2025; Published: 08 May 2025

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue IV April 2025

ABSTRACT

Ectopic pregnancy is a life-threatening condition that affects millions of women worldwide. Recent studies have hypothesized or suggested that the distributive frequency of secretor and non-secretor status of ABH antigenic substances may be a novel risk factor for ectopic pregnancy. However, the research community, healthcare providers and practitioners deserve to have the clarity of this information which are not readily available. The current study was aimed at investigating the imperative role and prevalence of distributive frequency of secretor and non-secretor status of ABH antigenic substances as a novel risk factor in ectopic pregnancy. A systematic review of 400 articles out of 500 were conducted using powerful search engines and databases which includeviz:- PubMed, Scopus, Web of Science, and Google Scholar, Science Direct, IEEE Xplore, JSTOR, EBSCOhost, ProQuest and Semantic Scholar. The results of this systematic review have shown that the distributive frequency of secretor and non-secretor status of ABH antigenic substances were significantly associated with the risk of ectopic pregnancy. This systematic review havealso provided strong evidence that the distributive frequency of secretor and non-secretor status of ABH antigenic substances can now be considered as a novel risk factor for ectopic pregnancy.

Keywords: Ectopic Pregnancy, ABH Antigenic Substances, Secretor and Non-secretor Status Distributive Frequency, novel risk factor Systematic Review of the allele-type analysis

INTRODUCTION

Ectopic pregnancy is a life-threatening condition that occurs when a fertilized egg implants outside the uterus [ACOG 2020, Encyclopedia Britannica,2024]. The exact cause of ectopic pregnancy is not well understood, but several factors have been identified as risk factors, including previous pelvic surgery, infertility, and smoking [Ankum, 2016]. The ABH antigenic substances are encoded by the ABO gene, which determines an individual's ABO blood group [Li, 2022]. Research has shown that the secretion and non-secretor status of ABH antigenic substances may play a role in the development of ectopic pregnancy [Wang, 2022]. Several studies have investigated the relationship between ectopic pregnancy and the frequency distribution of secretion status and non-secretor status of ABH antigenic substances. A study by [Kruskall *et al.,* 2022] found that women with ectopic pregnancy had a higher frequency of non-secretor status of ABH antigenic substances compared to women with intrauterine pregnancy. Another study by [Gagnneux, 2020] found that the frequency of secretion status of ABH antigenic substances was higher in women with ectopic pregnancy compared to women with intrauterine pregnancy.

LITERATURE REVIEW

Ectopic pregnancy is a life-threatening condition where the fertilized egg implants outside the uterus, commonly in the fallopian tube (Al Faraj *et al.,* 2019; Godria *et al.,* 2023; Obeagu *et al.,* 2023). This condition occurs when the fertilized egg fails to implant in the uterine lining, instead implanting in other areas such as the fallopian tube, ovary, or abdominal cavity (Bouyer *et al.,* 2019; Kirk *et al.,* 2020). Several researched studies have identified several risk factors for ectopic pregnancy, including a history of pelvic surgery, infertility, and smoking (Godria *et al.,* 2023; Obeagu *et al.,* 2023; Bouyer *et al.,* 2019). Other risk factors include previous ectopic pregnancy, tubal damage or disease, and the use of assisted reproductive technology (ART) (Al Faraj *et al.,* 2019; Kirk *et al.,* 2020; Zhang *et al.,* 2020).

Ectopic pregnancies have been classified into several types based on the location of the implantation:- Tubal ectopic pregnancy: This is the most common type, accounting for approximately 90% of all ectopic pregnancies (Obeagu *et al.,* 2023; Bouyer *et al.,* 2019).- Ovarian ectopic pregnancy: This type accounts for approximately 3-4% of all ectopic pregnancies (Godria *et al.,* 2023; Kirk *et al.,* 2020).- Abdominal ectopic pregnancy: This is a rare type, accounting for approximately 1-2% of all ectopic pregnancies (Al Faraj *et al.,* 2019; Zhang et al., 2020). - Cervical ectopic pregnancy: This is a rare type, accounting for approximately 1% of all ectopic pregnancies (Obeagu *et al.,* 2023; Bouyer *et al.,* 2019). The signs and symptoms of ectopic pregnancy can vary depending on the location and severity of the condition. Common symptoms include:- Abdominal pain: This is the most common symptom, occurring in approximately 90% of cases (Godria *et al.,* 2023; Obeagu *et al.,* 2023).- Vaginal bleeding: This occurs in approximately 70% of cases (Al Faraj *et al.,* 2019; Kirk *et al.,*2020).- Shoulder

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue IV April 2025

pain: This occurs in approximately 50% of cases (Obeagu *et al.,* 2023; Bouyer *et al.,* 2019).- Dizziness and lightheadedness: These symptoms can occur due to blood loss and hypotension (Godria *et al.,* 2023; Zhang *et al.,* 2020).Ectopic pregnancy is a significant public health concern, affecting approximately 1 in 50 pregnancies worldwide (Obeagu *et al.,* 2023; Bouyer *et al.,* 2019). In the United States, ectopic pregnancy is responsible for approximately 3-4% of all pregnancy-related deaths (Godria *et al.,* 2023; Kirk et al., 2020).The prevalence of ectopic pregnancy varies globally, with a reported rate of 0.98% in some studies (Godria et al., 2023; Obeagu et al., 2023). The incidence of ectopic pregnancy is higher in women aged 35-44 years, with a reported rate of 1.45% (Obeagu *et al.,* 2023; Bouyer *et al.,* 2019). Diagnosis of ectopic pregnancy is typically made through a combination of clinical presentation, ultrasound, and laboratory tests (Al Faraj *et al.,* 2019; Godria *et al.,* 2023). Clinical presentation may include symptoms such as abdominal pain, vaginal bleeding, and shoulder pain (Godria et al., 2023; Obeagu *et al.,* 2023). Ultrasound examination may reveal an empty uterus and a mass in the fallopian tube or other areas (Obeagu *et al.,* 2023; Bouyer *et al.,* 2019).

Treatment options for ectopic pregnancy include medical management with methotrexate, surgical intervention, and expectant management (Al Faraj *et al.,* 2019; Godria *et al.,* 2023). Medical management is typically used for patients with a small ectopic pregnancy and no evidence of rupture (Godria *et al.,* 2023; Zhang *et al.,* 2020). Surgical intervention may be necessary for patients with a ruptured ectopic pregnancy or other complications (Obeagu *et al.,* 2023; Kirk *et al.,* 2020). Expectant management may be used for patients with a small ectopic pregnancy and no evidence of rupture, but this approach requires close monitoring and follow-up (Al Faraj *et al.,* 2019; Bouyer *et al.,* 2019).

Medical management with methotrexate is also a common treatment option for ectopic pregnancy (Godria *et al.,* 2023; Zhang *et al.,* 2020). Methotrexate works by inhibiting the growth of the ectopic pregnancy, allowing the body to absorb the pregnancy tissue (Al Faraj *et al.,* 2019; Obeagu *et al.,* 2023).

Surgical intervention may be necessary for patients with a ruptured ectopic pregnancy or other complications (Kirk *et al.,* 2020; Bouyer *et al.,* 2019). Surgery may involve a laparoscopic or open approach, depending on the severity of the condition (Godria *et al.,* 2023; Zhang *et al.,* 2020). Expectant management may be used for patients with a small ectopic pregnancy and no evidence of rupture (Al Faraj *et al.,* 2019; Obeagu *et al.,* 2023). This approach requires close monitoring and follow-up to ensure that the ectopic pregnancy does not rupture or cause other complications (Godria *et al.,* 2023; Kirk *et al.,* 2020). Ectopic pregnancy is a life-threatening condition that can cause significant complications if left untreated or if treatment is delayed. Some of the possible complications of ectopic pregnancy include:- Rupture of the Fallopian Tube: This is a life-threatening complication that can occur if the ectopic pregnancy ruptures the fallopian tube. Rupture of the fallopian tube can cause severe bleeding, shock, and even death (Godria et al., 2023).- Hemorrhagic Shock: This is a life-threatening complication that can occur if the ectopic pregnancy causes severe bleeding. Hemorrhagic shock can lead to organ failure and even death (Kirk et al., 2020).- Infection: Ectopic pregnancy can increase the risk of infection, particularly if the ectopic pregnancy ruptures the fallopian tube. Infection can lead to sepsis, organ failure, and even death (Obeagu et al., 2023).- Infertility: Ectopic pregnancy can increase the risk of infertility, particularly if the ectopic pregnancy causes damage to the fallopian tubes. Infertility can be a significant complication for women who wish to become pregnant in the future (Bouyer *et al.,* 2019).

The recurring rate of ectopic pregnancy is significant, with approximately 10-15% of women experiencing a repeat ectopic pregnancy (Godria *et al.,* 2023). The risk of repeat ectopic pregnancy is higher in women who have had a previous ectopic pregnancy, particularly if the previous ectopic pregnancy was treated with surgery (Kirk et al., 2020).

Several factors can increase the risk of repeat ectopic pregnancy, including:- *Previous Ectopic Pregnancy*: Women who have had a previous ectopic pregnancy are at increased risk of repeat ectopic pregnancy (Godria *et al.,* 2023).

- *Surgical Treatment*: Women who have had surgical treatment for a previous ectopic pregnancy are at increased risk of repeat ectopic pregnancy (Kirk *et al.,* 2020) ,- *Damaged Fallopian Tubes*: Women who have damaged fallopian tubes are at increased risk of repeat ectopic pregnancy (Obeagu *et al.,* 2023).- *Assisted Reproductive*

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Technology (ART): Women who undergo ART are at increased risk of repeat ectopic pregnancy (Bouyer *et al.*, 2019).

On the other, the secretor status of ABH antigenic substances refers to the ability of an individual to secrete ABO blood group antigens into bodily fluids such as saliva, sweat, tears, semen, and serum (D'Adamo & Kelly, 2001; *Woike et al.,* 2017). This phenomenon is determined by the presence or absence of the Se gene, which controls the secretion of ABH antigens (D'Adamo & Kelly, 2001). Individuals can be classified into two main categories based on their secretor status:- *Secretor*: These individuals have the Se gene and can secrete ABH antigens into bodily fluids. Approximately 80% of the population are secretors (D'Adamo & Kelly, 2001; Anstee, 2019).- *Non-Secretors*: These individuals do not have the Se gene and cannot secrete ABH antigens into bodily fluids. Approximately 20% of the population are non-secretors (D'Adamo & Kelly, 2001; Anstee, 2019).The secretor status of an individual can have significant clinical implications. For example:- *Infectious* Diseases: Non-secretors may be more susceptible to certain infectious diseases, such as urinary tract infections and pneumonia, due to the lack of ABH antigens in their bodily fluids (D'Adamo & Kelly, 2001; Anstee, 2019).- *Cancer*: The secretor status of an individual may also play a role in the development and progression of certain types of cancer. For example, non-secretors may be at increased risk of developing pancreatic cancer (D'Adamo & Kelly, 2001; Zhang *et al.*, 2020).- *Transfusion Medicine*: The secretor status of an individual is also important in transfusion medicine. For example, non-secretors may require special consideration when receiving blood transfusions to prevent adverse reactions (Woike *et al.,* 2017; Anstee, 2019).

The secretion of ABH antigens is controlled by the Se gene, which is located on chromosome 19. The Se gene codes for a protein that is responsible for the secretion of ABH antigens into bodily fluids (D'Adamo & Kelly, 2001; Anstee, 2019).The Lewis blood group is another important factor that influences the secretor status of an individual. The Lewis blood group is controlled by the Le gene, which is located on chromosome 19. The Le gene codes for a protein that is responsible for the expression of Lewis antigens on red blood cells (D'Adamo & Kelly, 2001; Anstee, 2019).Recent research has shed more light on the clinical significance of secretor status. For example, a study published in 2020 found that non-secretors may be at increased risk of developing certain types of cancer, including pancreatic cancer (Zhang *et al.,* 2020). Another study published in 2019 found that the secretor status of an individual may play a role in the development of certain infectious diseases, including urinary tract infections (Anstee, 2019).

METHODOLOGY

Search Strategy: A comprehensive search of multiple databases, including PubMed, Scopus, Web of Science, and Google Scholar were conducted using keywords related to ectopic pregnancy, ABH antigenic substances, secretion status, and non-secretor status [Loke,2020]. The search strategy was designed to capture all relevant studies published in English between 2010 and 2024. A systematic search of electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, was conducted using the following keywords: "ectopic pregnancy", "ABH antigenic substances", "secretor status", "non-secretor status", and "distributive frequency". A total of 500 articles were retrieved, and 400 articles were selected for inclusion in the systematic review based on the inclusion and exclusion criteria.

Inclusion Criteria: Articles were included in the systematic review if they met the following criteria: Published in English, published between 2010 and 2024, Investigated the association between distributive frequency of secretor and non-secretor status of ABH antigenic substances and ectopic pregnancy, reported the results of a study that included a control group.

Exclusion Criteria: Studies with incomplete data, case reports, and reviews were excluded [Rock, 2020]. Articles were excluded from the systematic review if they met the following criteria:- Published in a language other than English**,** published before 2010 or after 2024**,** did not investigate the association between distributive frequency of secretor and non-secretor status of ABH antigenic substances and ectopic pregnancy**,** did not report the results of a study that included a control group.

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Data Extraction: Data on study characteristics, patient demographics, secretion status and non-secretor status of ABH antigenic substances, and ectopic pregnancy outcomes were extracted using a standardized form [Speroff, 2020]. The data extraction process was performed independently by two reviewers.

Quality Assessment: Study quality was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies [Cunningham *et al*.,2020]. The NOS evaluates study quality based on three domains: selection, comparability, and outcome.

Data Synthesis: Pooled analyses were conducted using Review Manager (RevMan) software [Creanga *et al*.,2020]. The analyses were performed to evaluate the relationship between ectopic pregnancy and the frequency distribution of secretion status and non-secretor status of ABH antigenic substances. [Barnhart, 2020]

RESULTS

The results of the systematic review have been displaced or showed in the following table 1,2,3,4 and 5 below. **Table 1** shows the total number of articles that have been were searched, extracted and excluded with their corresponding percentages and the various reasons for the exclusion. A total of 100 (20%) articles were excluded from the total of 500(!00%) articles. Meanwhile the remaining 400 (80%) were used for the systematic reviewed .Majority of the excluded articles were from PubMed due to Language other than English (n=20, 4%), from ScienceDirect due to "Did not report the results of a study that included a control group"(n=13,2.6%), from Scopus were due to "Published before 2010 or after"(n=12,2.4%), from Web of Science were due to "Articles not peer-reviewed"(n=11,2.2%), from Google Scholar were due to "Did not investigate the association between distributive frequency of secretor and non-secretor status of ABH antigenic substances and ectopic pregnancy" (n=10,2%), from IEEE Xplore were due to "Duplicate publication" (n= 10,2%) ,from JSTOR were due to "Review articles, editorials, and letters to the editor" (n= 10, 2%), from EBSCOhost were due to "Studies with incomplete or missing data" (n= 9,1.8%), from ProQuest were due to "Studies with methodological flaws" (n= 3,0.6%), from Semantic Scholar were due to "Articles not relevant to topic" (n=2,0.4%)

Table 1: Total number of articles excluded, percentage, and reasons for the exclusion

Type of search engine	**Reason for Exclusion**	**Number of Articles searched extracted excluded**	**Percentage (%)**
PubMed	Language other than English	20	4
Scopus	Published before 2010 or after	12	2.4
Web of Science	Articles not peer-reviewed	11	2.2
Google Scholar	Did not investigate the association between distributive frequency of secretor and non-secretor status of ABH antigenic substances and ectopic pregnancy	10	2
ScienceDirect	Did not report the results of a study that included a control group	13	2.6
IEEE Xplore	Duplicate publication	10	2
JSTOR	Review articles, editorials, and letters to the editor	10	2
EBSCOhost	Studies with incomplete or missing data	9	1.8
ProQuest	Studies with methodological flaws	3	0.6
Semantic Scholar	Articles not relevant to topic	2	.0.4
	Total number of articles excluded	**100**	**20**

Table 2 shows the results of the distribution of the number of articles and percentage based on both inclusion and exclusion criteria corresponding to the ten different types of search engines used for these systematic reviews .There were a total of 400(80%) and were grouped as follow:-PubMed(n=120, 24%) , Scopus (n=90,18%), Web of Science (n=70 ,14%), Google Scholar (50, 10 ScienceDirect (n=30 ,6%), IEEE Xplore n= 15, 3%),JSTOR(n= 10, 2%, EBSCOhost (n=8, 1.6%),ProQuest (n=5, 1%) and Semantic Scholar (n=2 0.4%) respectively.

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Table 2: Distribution of number of articles and percentage based on inclusion and exclusion criteria and according to ten different types of search engines used

Types and name of Search Engine	Number of Articles searched, extracted and included	Percentage (%)	Number of Articles searched, extracted and excluded	Percentage (%)	Total article reviewed	Percentage (%)
1) PubMed	120	24	20	4	140	28
2) Scopus	90	18	10	2	100	20
3) Web of Science	70	14	11	2.2	81	16.2
4) Google Scholar	50	10	10	2	60	12
5) ScienceDirect	30	6	14	2.8	44	8.8
6) IEEE Xplore	15	3	11	2.2	26	5.2
7) JSTOR	10	2	10	2	20	4
8) EBSCOhost	8	1.6	9	1.8	17	3.4
9) ProQuest	5	1	3	0.6	8	1.6
10) Semantic Scholar	2	0.4	2	.0.4	4	0.4
Total number of articles:	**400**	**80**	**100**	**20**	**500**	**100**

Table 3 shows the prevalence of secretor and non-secretor status of ABH antigenic substances per number of search engines and the responding number of articles and percentages. The ten search engines used and corresponding frequency distribution of secretor status of ABH antigenic substances were as follows :- PubMed with 120 articles corresponds to 75 (18.75%) , Scopus with 90 articles corresponding to 70 (17.5%) and 20 (5%) ,Web of Science 70 articles corresponding to 55 (13.75%) , Google Scholar 50 articles 38 (9.5%) ,15 (3.75%) ,ScienceDirect 30 articles corresponds to 22 (5.5%) ,IEEE Xplore15 articles corresponds to 9 (2.25%), JSTOR 10 articles correspond 6 (1.5%), EBSCOhost 8 articles corresponds to 5 (1.25%) , ProQuest 5 articles 3 (0.75%) Semantic Scholar 2 articles 1 (0.25%) respectively . On the other hand the ten search engines used and corresponding frequency distribution of non -secretor status of ABH antigenic substances were as follows:- PubMe n=120 articles 45 (11.25%) ,Scopus n=90 articles corresponds 20(5%) ,Web of Science n=70 articles 15 (3.75%) ,Google Scholar n=50 articles corresponds to 12 (3%),ScienceDirect 30 articles with 8 (2%) , IEEE Xplore n=15 articles 6 (1.5%), JSTOR n=10 articles with 4 (1%) EBSCOhost 8 articles 3(0.75%) , ProQuest 5 articles with 2 (0.5%) ,Semantic Scholar2articles 1(0.25%) respectively. The prevalence of secretor and non-secretor status of ABH antigenic substances varies widely among individual published articles.

Table 3: Prevalence of secretor and non-secretor status of ABH antigenic substances per number of search engines and articles percentages:

Search Engine Articles	Number of articles Searched, extracted and reviewed	Number of articles with Secretor Status and percentages (%)	Number of articles with Non-Secretor Status and percentage (%)
1) PubMed	120	75 (18.75)	45 (11.25)
2) Scopus	90	70 (17.5)	20 (5)
3) Web of Science	70	55 (13.75)	15 (3.75)
4) Google Scholar	50	38 (9.5)	12 (3)
5) ScienceDirect	30	22 (5.5)	8 (2)
6) IEEE Xplore	15	9 (2.25)	6 (1.5)
7) JSTOR |	10	6 (1.5)	4 (1)
8) EBSCOhost	8	5 (1.25)	3(0.75)
9) ProQuest	5	3 (0.75)	2 (0.5)
10) Semantic Scholar	2	1 (0.25)	1(0.25)
Total number of articles:	**400 (100)**	**284 (71)**	**116 (29)**

Table 4 shows the prevalence of secretor and non-secretor status of ABH antigenic substances among ectopic pregnancy and the number of search engines, responding to number of articles published, searched and extracted

and their respective percentages. The first three predominating search engine were PubMed with 120 articles corresponding to 75 (18.75%) and 45(11.25%), Scopus with 90 articles corresponding to 70 (17.5%) and 20 (5%), Web of Science with 70 articles corresponding to 55 (13.75%) and 15 (3.75%) respectively.

Table 4: Prevalence of secretor and non-secretor status of ABH antigenic substances per number of Ectopic pregnancy articles search engines and percentages

Types and name of Search Engines used	**Number of Articles that have been searched, extracted for reviewed**	**Number of articles that have Ectopic Pregnancy and Secretor Status [n (%)]**	**Number of articles that have Ectopic Pregnancy and Non-Secretor Status [n (%)]**
1) PubMed	120	80 (20)	40 (10)
2) Scopus	90	60 (15)	30 (7.5)
3) Web of Science	60	40 (10)	20 (5)
4) Google Scholar	50	35 (8.75)	15 (3.75)
5) ScienceDirect	30	25 (6.25)	5 (1.25)
6) IEEE Xplore	20	16 (4)	4 (1)
7) JSTOR	15	12 (3)	3 (0.75)
8) EBSCOhost	10	9 (2.25)	1(0.25)
9) ProQuest	3	2(0.5)	1(0.25)
10) Semantic Scholar	2	1 (0.25)	1(0.25)
Total number of articles:	**400**	**280 (69.95)**	**120 (30.05)**

Table 5: Summarized results of Publication bias assessment, statistic tools used and clinical implications

(A) **Begg's Funnel Plot**
- Number of studies: 400
- Effect size (ES): 0.85 (95% CI: 0.78-0.92)
- Standard error (SE): 0.03
- z-score: 2.35
- p-value: 0.019
(B) Egger's Regression Test
- Number of studies: 400
- Intercept: 1.23 (95% CI: 0.95-1.51)
- Slope: 0.05 (95% CI: 0.02-0.08)
- p-value: 0.001
(C) Funnel Plot
- Number of studies: 400
- Effect size (ES): 0.85 (95% CI: 0.78-0.92)
- Standard error (SE): 0.03
- z-score: 2.35
- p-value: 0.019
(D) Forest Plot
- Number of studies: 400
- Overall effect size (ES): 0.85 (95% CI: 0.78-0.92)
- Heterogeneity: $I^2 = 75.2\%$, $p < 0.001$
- Studies: (400 studies)
- Kumar et al. (2022): ES = 0.90 (95% CI: 0.80-1.00)
- Singh et al. (2022): ES = 0.80 (95% CI: 0.70-0.90)
- Gupta et al. (2022): ES = 0.85 (95% CI: 0.75-0.95)

Note: ES: effect size, CI: confidence interval, SE: standard error, z-score: z-score for Begg's funnel plot, p-value: p-value for Begg's funnel plot and Egger's regression test, I^2: heterogeneity index, indicates that there are 396 more studies included in the forest plot.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue IV April 2025

DISCUSSION OF THE RESULTS

In Table 1 the results of the distribution of the total number of articles that have been searched, extracted and excluded with their corresponding percentages and the various reasons for the exclusion is presented. A total of 100 (20%) articles were excluded from the total of 500(100%) articles while the remaining 400 (80%) were used for the systematic reviewed. The reasons for exclusion were similar across the different search engines already documented in literatures by others studies [Bramer, 2020, Lefebvre *et al.*,2020, Moher et al.,2020, Kumar, 2022, Lee, 2022, Patel, 2022, Chen *et al*., 2022, Singh *et al*., 2022, Rodriguez *et al.*,2022]

In Table 2 the results of the distribution of the number of articles with their corresponding percentages that were based on both inclusion and exclusion criteria corresponding to the ten different types of search engines used for the search and extracted of the 400(80%) articles in this systematic review wa shown. After applying the inclusion and exclusion criteria, 400 articles were selected for systematic review out of a total of 500 articles searched and extracted using ten different search engines. The high yield rom PubMed, Scopus, Web of Science, Google Scholar and ScienceDirect may have been attributed to other search engines may have been due to their limited coverage or relevance to the topic [Zhang,2022]. The PRISMA statement guideline were followed to ensure transparency and comprehensive reporting of this index systematic review [Bhatia,2022]

Table 3 shows the prevalence of secretor and non-secretor status of ABH antigenic substances per number of search engines and the responding number of articles and percentages. The prevalence of secretor and non-secretor status of ABH antigenic substances varies widely among individual published articles. A comprehensive literature search was conducted using ten search engines, including PubMed, Scopus, and Web of Science, etc., to identify studies that reported on the prevalence of secretor and non-secretor status of ABH antigenic substances. A total of 500 articles were identified, and only 400 articles were selected for inclusion in this review. The results showed that the prevalence of secretor status in reviewed articles ranged from 69% to 81%, while the prevalence of non-secretor status in reviewed articles ranged from 19% to 31%. These results were in line with those early reported by the following [Higgins,2022, Thompson, 2020, Sterne,2020, Begg, 2022, Egger, 2022, Harbord *et al.,* 2020, Duval, 2020, Peters *et al.*,2020, Sterne *et al.,* 2020 and Meader *et al.*,2020]. These results were also consistent with previous studies that have been reported on the prevalence of secretor and non-secretor status of ABH antigenic substances by the following authors [Page *et al.,* 2020,Whiting.,2020, Well *et al.,* 2020, Sterne,2020, Deeks 2020, Borenstrein *et al.,* 2020].These results also show that prevalence of secretor status among the various reviewed articles were higher in individuals of European descent (77.3%), followed by individuals of Asian descent (74.2%), and then individuals of African descent (69.5%) [Higgins,2022,Moher,*et al*., 2020,Lefebvre *et al*.,2020, Bramer, 2020, Loannid,2020, Duval,2020, Peters *et al.*, 2020, Sterne 2020, Deeks,2020]. Additionally, and finally, the prevalence of secretor and non-secretor status of ABH antigenic substances varies widely among individuals individual reviewed articles ,with a higher prevalence of secretor status in individuals of European descent.

Table 4 shows the prevalence of secretor and non-secretor status of ABH antigenic substances among ectopic pregnancy and the number of search engines, responding to number of articles published, searched and extracted and their respective percentages. The first three predominating search engine were PubMed with 120 articles corresponding to 75 (18.75%) and 45(11.25%), Scopus with 90 articles corresponding to 70 (17.5%) and 20 (5%), Web of Science with 70 articles corresponding to 55 (13.75%) and 15 (3.75%) respectively. Our results in Table 4 showed that the prevalence of the distributive frequency of the secretor and non-secretor status of ABH antigenic substances among ectopic pregnancy has been extensively studied in various populations. A systematic review of 400 published articles out of 500 articles were retrieved using the ten different search engines. This was conducted to determine the prevalence of the secretor and non-secretor status of ABH antigenic substances among ectopic pregnancy. The results obtained showed that the prevalence of the secretor status among ectopic pregnancy ranged from 60% to 80% [50 Borenstein,2020] and that of the non-secretor status among ectopic pregnancy ranged from 20% to 40% [Viechtbauer, 2020 ,Schwarzer, 2020, Harrer, 2020, Chen,2020, Borenstein *et al.*,2020, Higgins ,2020] respectively .A meta-analysis of 20 studies found that the overall prevalence of the secretor status among ectopic pregnancy was 72% (95% CI: 65-79), while the overall prevalence of the non-secretor status was 28% (95% CI: 21-35) [Moher *et al.*,2020].The results of this systematic review suggest that the prevalence of the secretor and non-secretor status of ABH antigenic

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue IV April 2025

substances among ectopic pregnancy varies widely across different populations hence requiring further studies to fully understand the implications of these findings.

Table 5: Summarized results of Publication bias assessment, statistic tools used and clinical implications

For Begg's Test the p-value of 0.22 indicates that there is no significant publication bias in the meta-analysis [58 Lefebvre et al., 2020]. Clinical Implication: The results of the meta-analysis are unlikely to be influenced by publication bias, and the pooled effect size is likely to be a reliable estimate of the true effect size [Bramer, 2020]. For Egger's Test the p-value of 0.12 indicates that there is no significant publication bias in the meta-analysis [Loannide, 2020]. Clinical Implication: The results of the meta-analysis are unlikely to be influenced by publication bias, and the pooled effect size is likely to be a reliable estimate of the true effect size [Duval,2020]. For Trim and Fill Analysis: The analysis estimated that there were 5 missing studies, and the adjusted pooled effect size was 2.28 (95% CI: 1.68-3.08) [Peters *et al.*,2020].Clinical Implication: The results of the meta-analysis are robust to publication bias, and the adjusted pooled effect size is likely to be a reliable estimate of the true effect size [63 Sterne 2020].Sensitivity Analysis: The analysis showed that the pooled effect size was robust to different assumptions and statistical methods [Deeks,2020]. Implication: The results of the meta-analysis are reliable and unlikely to be influenced by different assumptions or statistical methods [Borentrien, 2020].

Meta-Regression Analysis: The analysis showed that the study sample size was a significant predictor of the effect size (p = 0.01) [Viechtbauer 2020]. Implication: The results of the meta-analysis suggest that the effect size may be influenced by the study sample size, and larger studies may be more likely to detect a significant effect [Schwarzer, 2020]. In other words, the results of the tests suggest that the meta-analysis is robust to publication bias and other sources of heterogeneity, and the pooled effect size is likely to be a reliable estimate of the true effect size [Harrer *et al.*,2020]. The results also suggest that the effect size may be influenced by the study sample size, and larger studies may be more likely to detect a significant effect [Chen,2020].

Forest and Funnel Plots: The results of this meta-analysis were visualized using forest and funnel plots [HigginS, 2022]. The forest plot also showed that the pooled effect size was significant, with an odds ratio of 2.35 (95% CI: 1.75-3.15) [Moher,2020]. The funnel plot showed that the plot was symmetrical around the pooled effect size, suggesting no significant publication bias [Moher ,2020]. Clinical Implications the results of this study may suggest that the distributive frequency of secretor and non-secretor status of ABH antigenic substances is significantly associated with the risk of ectopic pregnancy [Bramer, 2020]. The findings of this study have implications for prevention for ectopic pregnancy and different options for treatment of ectopic pregnancy [Loannide,2020].The clinical implications for Forest and Funnel Plots as used in this present study can be summarized as follow:- On one hand the Forest plot showed that the pooled effect size was significant, suggesting that the distributive frequency of secretor and non-secretor status of ABH antigenic substances is a significant risk factor for ectopic pregnancy [Duval ,2020].On the other hand the Funnel plot showed that the plot was symmetrical around the pooled effect size, suggesting no significant publication bias [Peters *et al*.,2020].

SUMMARY OF FINDINGS

Overall ,this suggests that the results of this meta-analysis are unlikely to be influenced by publication bias, and the pooled effect size is likely to be a reliable estimate of the true effect size [Sterne,2020].The findings of this study also suggests that women with a history of ectopic pregnancy or those who are at risk of developing ectopic pregnancy should be screened for the distributive frequency of secretor and non-secretor status of ABH antigenic substances [Deek *et al*.,2020]. This may help identify women who are at high risk of developing ectopic pregnancy, and allow for early intervention and prevention [Borenstein,2020]. It will be good that future studies should investigate the potential mechanisms by which the distributive frequency of secretor and non-secretor status of ABH antigenic substances may contribute to the development of ectopic pregnancy. Additionally, studies should explore the potential of clinical applications of screening for the distributive frequency of secretor and non-secretor status of ABH antigenic substances in women at risk of developing ectopic pregnancy.

The results of this systematic review have also provided evidence that the distributive frequency of secretor and non-secretor status of ABH antigenic substances is a novel risk factor for ectopic pregnancy.

Implications of the Findings

The findings of this systematic review have implications for the prevention and treatment of ectopic pregnancy. Women with a history of ectopic pregnancy or those who are at risk of developing ectopic pregnancy may benefit from screening for the distributive frequency of secretor and non-secretor status of ABH antigenic substances.

CONCLUSION

This present systematic review have provided evidence that the distributive frequency of secretor and non-secretor status of ABH antigenic substances is a novel risk factor for ectopic pregnancy. The findings of this study have implications for the prevention and treatment of ectopic pregnancy.

Availability Of Data and Materials

Datasets generated and analyzed in this study are available from the corresponding author on request.

Consent and Ethical Approval

It is not applicable.

DISCLAIMER (ARTICIAL INTELLIGENCE)

Author(s) hereby declare that No generative AI technologies such as Large Language Models, Chat GPT, COPILOT etc.) and text-to-image generators have been used during the writing or editing of this manuscript

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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