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UTERINE FACTOR INFERTILITY: A MAJOR ISSUE OF THE PRESENT AGE

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Article Info

Abstract

Uterine Factor Infertility (UFI) represents a definitive and challenging subtype of female infertility, characterized by the uterus itself being the principal barrier to gestation. It encompasses Absolute UFI (AUFI), involving anatomical absence, and Non-Absolute UFI (NAUFI), involving a nonfunctional uterus. This systematic review synthesizes current evidence on the epidemiology, etiologies, and treatment landscape of UFI. Despite its clinical significance, reliable population-based and age-stratified prevalence data, particularly for women under 40, remain scarce. A key finding is the variable prevalence of hysterectomy—a major cause of AUFI—ranging from 1.70% to 10.0% in international studies. Congenital anomalies, intrauterine pathologies, and iatrogenic damage constitute other primary causes. For women with AUFI, traditional paths to biological parenthood are limited to adoption or surrogacy. Uterus transplantation (UTx) has emerged as a pioneering, albeit experimental, treatment offering the potential for gestation, with over 50 live births reported globally. However, significant surgical, immunosuppressive, and ethical challenges persist. This review underscores the urgent need for robust epidemiological studies to guide resource allocation and highlights UTx as a dynamic frontier in restoring reproductive potential for this patient population.

Keywords: Uterine Factor Infertility, Absolute Uterine Factor Infertility, Uterus Transplantation, Hysterectomy, Prevalence, Mayer-Rokitansky-Küster-Hauser Syndrome, Reproductive Medicine.

1. Introduction

Infertility, defined clinically as the failure to achieve a pregnancy after 12 months of regular, unprotected intercourse, is a pervasive global health issue with profound personal and societal consequences. Epidemiological studies consistently indicate that it impacts approximately 15-20% of couples, translating to an average of one in five couples during their reproductive lifespan [1]. This high prevalence underscores its status as a significant public health problem, associated with substantial psychological distress, social stigma, and economic burden on healthcare systems. The condition is further categorized based on obstetric history; primary infertility, where no prior conception has ever occurred, accounts for roughly one-third of cases, while secondary infertility, the inability to conceive following a previous successful pregnancy, constitutes the remaining two-thirds [2,3]. This distribution suggests a critical role for acquired factors, including aging, the development of new medical conditions, or complications from earlier pregnancies or surgeries. The etiology of infertility is multifactorial, originating from female factors (e.g., ovulatory disorders, tubal obstruction), male factors (e.g., impaired spermatogenesis, obstructive azoospermia), a combination of both, or remains unexplained in about 10% of cases despite comprehensive diagnostic evaluation, pointing to potential immunological, genetic, or molecular underpinnings not yet fully characterized [4].

A particularly definitive and challenging subtype within female-factor infertility is Uterine Factor Infertility (UFI), where the uterus itself is the principal barrier to gestation. UFI is formally classified into two distinct entities: Absolute Uterine Factor Infertility (AUFI), which denotes the complete anatomical absence of the uterus either congenitally, as in Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, or due to surgical removal (hysterectomy); and Non-Absolute Uterine Factor Infertility (NAUFI), which describes a present but irreparably damaged or nonfunctional uterus incapable of supporting implantation and pregnancy to term [5]. The exact population prevalence of UFI remains elusive due to diagnostic heterogeneity and regional reporting disparities, but early and frequently cited estimates propose it may affect 3–5% of women worldwide, with AUFI specifically impacting up to 1 in 500 women of childbearing age [5,6]. The causes of UFI are diverse, spanning congenital and acquired pathologies. Congenital causes primarily include uterine agenesis and severe Müllerian duct malformations. Acquired causes encompass surgical removal via hysterectomy, benign intra-cavitary distortions from polyps or leiomyomas (myomas), infiltrative conditions like adenomyosis, the formation of intrauterine scar tissue (synechiae or Asherman's syndrome), and irreversible endometrial damage from pelvic or uterine irradiation for cancer therapy [7,8]. A critical gap in the current literature, as highlighted by this review, is the notable absence of reliable, age-stratified epidemiological data. Specifically, there is a lack of robust population-based studies detailing the precise prevalence of UFI and the distribution of its various etiologies among women under the age of 40, which hinders targeted resource allocation and research [9].

For women diagnosed with AUFI, the traditional pathways to biological parenthood are severely constrained. Options are essentially limited to adoption or gestational surrogacy where legally and ethically permitted, the latter of which involves complex logistical, financial, and psychosocial considerations. This profound therapeutic limitation has propelled uterus transplantation (UTx) from a theoretical concept into a pioneering clinical reality. Although still formally considered an experimental procedure within the research stage, UTx has evolved rapidly since the first live birth from a transplanted

uterus in 2013. It represents a paradigm-shifting intervention that offers the potential for women with AUFI to experience pregnancy and childbirth [10]. The procedure involves the surgical implantation of a uterus from a living or deceased donor, followed by in vitro fertilization (IVF) using the recipient's own oocytes, embryo transfer, and ultimately, a carefully monitored pregnancy culminating in a cesarean delivery. While over 90 procedures have been performed globally resulting in more than 50 live births, significant challenges persist, including the risks of major surgery, lifelong immunosuppression, graft rejection, and ethical concerns regarding donor risk and allocation. Nevertheless, UTx stands as the only treatment that can restore uterine function and the gestational experience, solidifying its position as a beacon of hope and a dynamic frontier in reproductive medicine for this specific patient population [10].

Materials and Methods

Search Strategy

A systematic literature search was conducted in accordance with PRISMA(Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparency and reproducibility. The databases PubMed/MEDLINE, Google Scholar, and Scopus were comprehensively searched from their inception until a final search date of [Insert Date, e.g., June 2025]. The search strategy employed a combination of Medical Subject Headings (MeSH) and free-text keywords, including core terms such as "uterine factor infertility," "absolute uterine factor infertility (AUFI)," "Mayer-Rokitansky-Küster-Hauser syndrome," "prevalence," "etiology," and "uterus transplantation." Boolean operators (AND, OR) were used to link concept blocks, and the strategy was tailored to the syntax of each database to maximize sensitivity.

Inclusion and Exclusion Criteria

Studies were selected based on predefined criteria to maintain focus and relevance. The review included original observational studies (e.g., cohort, cross-sectional) and clinical trials that reported quantitative or qualitative data on the epidemiology, causes, or treatment outcomes of UFI in human females of reproductive age. Exclusion criteria were applied to remove non-research publications such as reviews, editorials, and case reports, as well as studies not specifically focused on uterine-factor pathology or those where the full text was unavailable, ensuring the synthesis was based on robust, primary evidence.

Study Selection & Data Extraction

The selection process was designed to minimize bias. Identified records were collated, and duplicates were removed. A two-stage screening was then performed independently by two reviewers. First, titles and abstracts were screened against the criteria. Second, the full texts of potentially eligible studies were retrieved and assessed in detail for final inclusion. Any disagreements between reviewers were resolved through discussion or by consulting a third researcher, ensuring a consensus-based selection. Critical data from each included study were systematically extracted using a piloted, standardized form to ensure consistency. Key extracted information included study characteristics (author, year, country, design), population details (sample size, age), UFI-specific data (diagnostic criteria, prevalence, etiological breakdown), and intervention outcomes (where applicable, such as transplant success or complication

rates). This structured approach facilitated the subsequent organization and comparison of findings across the diverse literature.

Data Synthesis

Given the anticipated heterogeneity in study designs, populations, and UFI definitions, a quantitative meta-analysis was not feasible. Therefore, the findings were synthesized using a qualitative narrative synthesis approach. The results were thematically organized to address the core review questions on prevalence, etiology, and treatment landscapes. To appraise the methodological quality and risk of bias of the included observational studies, the Newcastle-Ottawa Scale (NOS) was employed, providing a critical lens through which to interpret the strength of the accumulated evidence.

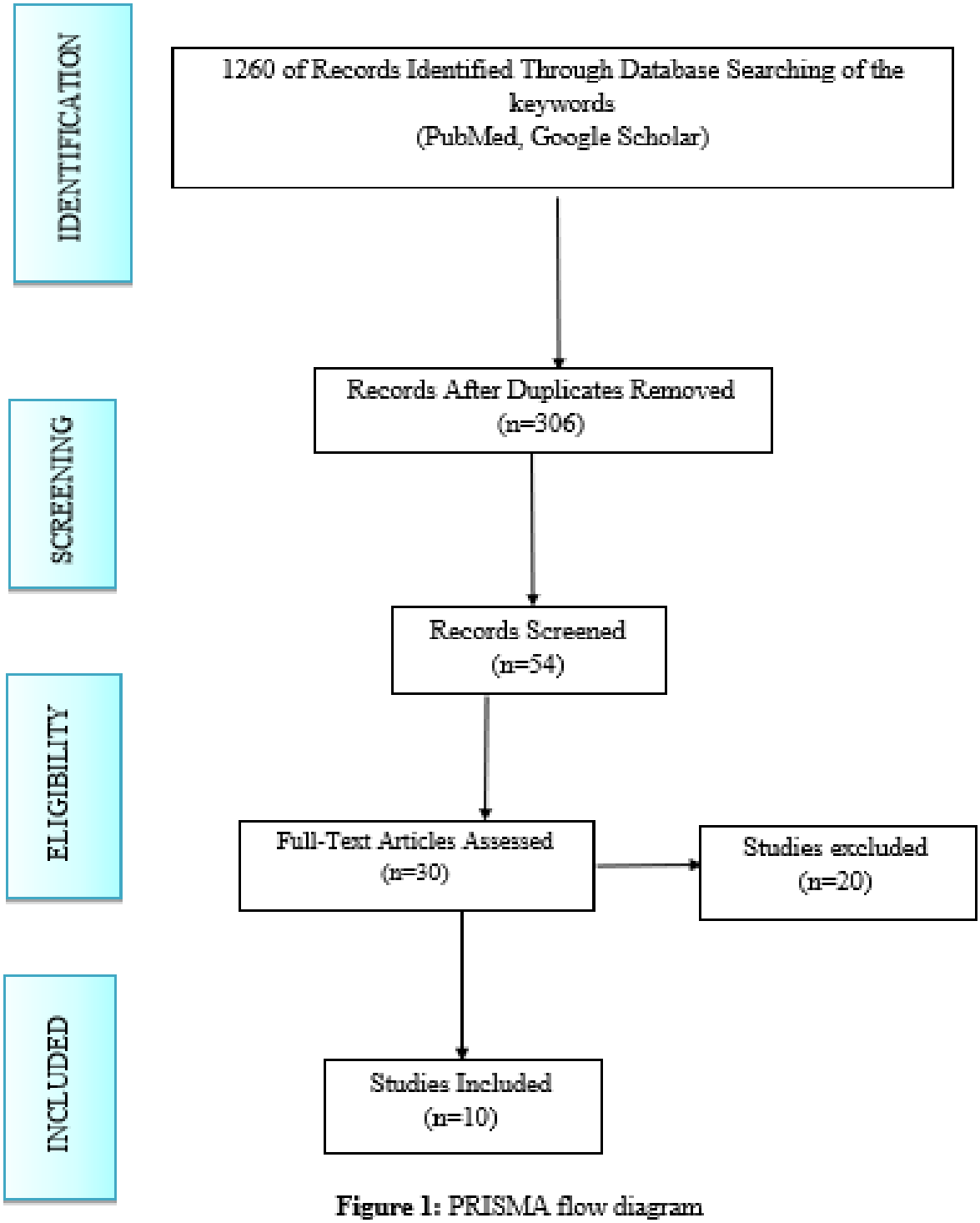

Figure 1: PRISMA flow diagram

RESULTS

The systematic search and selection process, detailed in the PRISMA flow diagram (Figure 1), yielded studies for qualitative synthesis. A primary focus was the prevalence of hysterectomy in women under 40 years of age, a key surrogate and causative factor for Absolute Uterine Factor Infertility (AUFI). As summarized in Table 1, the reported prevalence varied significantly across different geographical regions and study designs, ranging from 1.70% in a cross-sectional study in India to 10.0% in retrospective studies from the USA and Scotland. This wide range highlights substantial international and methodological heterogeneity. Data specifically quantifying the prevalence of non-absolute uterine factor causes (e.g., severe Asherman's syndrome, irreparable Mullerian anomalies) in this age group were notably absent from the identified literature. Furthermore, no studies provided a comprehensive, age-stratified epidemiological breakdown of all UFI etiologies within the targeted reproductive-age population.

Table 1: Prevalence of Hysterectomy in Women Under Age 40.

Sr. No.	Author	Publication Year	Study Desigy	Country	Prevalence (%)
1	Gartner et al. [11]	**2020**	**Retrospective**	**USA**	**6.0**
2	Meher et al. [12]	2020	Retrospective	India	4.10
3	Shekhar et al. [13]	**2019**	**Cross-sectional**	**India**	**4.8**
4	Unzurrunzaga et al. [14]	**2019**	**Retrospective**	**Scotland**	**10.0**
5	Desai et al. [15]	**2019**	**Cross-sectional**	**India**	**3.59**
6	Temkin et al. [16]	**2018**	**Retrospective**	**USA**	**10.0**
7	Prusty et al. [17]	**2018**	**Cross-sectional**	**India**	**1.70**
8	Liu et al. [18]	**2017**	**Cross-sectiona**	**China**	**3.32**
9	Rositch et al. [19]	**2014**	**Retrospective**	**USA**	**10.0**
10	Bower et al. [20]	**2010**	**Retrospective**	**USA**	**10.0**

DISCUSSION

The findings of this review highlight a critical gap in the understanding of Uterine Factor Infertility (UFI): the lack of precise, age-stratified epidemiological data. The significant variance in hysterectomy prevalence among women under 40 (1.70%-10.0%) underscores the influence of regional healthcare

practices, cultural factors, and indication trends. This variability complicates global burden estimation and targeted health policy planning for AUFI.

The absence of robust data on NAUFI etiologies further impedes a complete understanding of the UFI landscape. Conditions like severe intrauterine adhesions, adenomyosis, and congenital malformations other than agenesis likely contribute substantially to infertility but are poorly quantified in population studies. This gap hinders the development of preventive strategies and non-transplant treatment protocols.

Uterus transplantation (UTx) has undeniably transformed the therapeutic horizon for AUFI, moving from theory to clinical reality with over 50 live births. It is the sole intervention capable of restoring uterine function and the gestational experience. However, its current status as an experimental procedure is warranted. Major challenges include the inherent risks of complex vascular surgery, the necessity for lifelong immunosuppression with its attendant risks of infection, metabolic complications, and potential malignancy, the risk of graft rejection or failure, and substantial ethical considerations regarding donor risk-benefit balance and equitable access.

Future research must prioritize large-scale, multinational studies to establish the true prevalence and etiological distribution of UFI in women of reproductive age. Concurrently, longitudinal studies on UTx outcomes are essential to refine surgical techniques, optimize immunosuppression regimens, and fully understand the long-term health implications for recipients and children. Addressing these knowledge deficits is crucial for evidence-based counseling, equitable resource allocation, and advancing safe and effective treatments for women with UFI.

CONCLUSION

Uterine Factor Infertility is a complex condition that presents a profound challenge to affected women desiring biological parenthood. This systematic review confirms that while hysterectomy prevalence data offer some insight, comprehensive and age-specific epidemiological data on UFI are severely lacking. The etiological spectrum is broad, encompassing both congenital and acquired uterine pathologies. For women with Absolute UFI, uterus transplantation stands as a groundbreaking medical advance, offering unprecedented hope. Nevertheless, it remains a procedure weighed down by significant medical risks and ethical complexities. To improve care for this population, the field must urgently address the epidemiological data deficit and continue rigorous clinical research to enhance the safety, efficacy, and accessibility of UTx. Ultimately, a multifaceted approach combining accurate epidemiology, preventive gynecology, and responsible innovation in transplant medicine is essential to address the needs of women with uterine factor infertility.

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