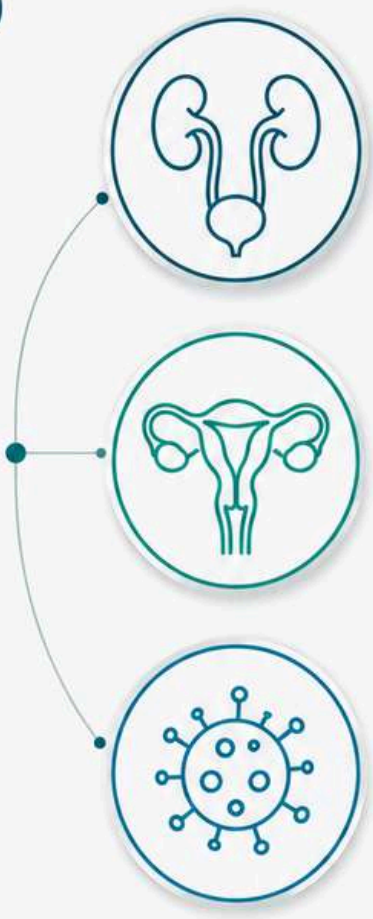
INTEGRATIVE APPROACHES IN MEDICAL SCIENCES:

UROLOGY, WOMEN'S HEALTH, AND INFECTIOUS CONDITIONS



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INTEGRATIVE APPROACHES IN MEDICAL SCIENCES: UROLOGY, WOMEN'S HEALTH, AND INFECTIOUS CONDITIONS

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PREFACE

Medical and health sciences encompass a wide range of research areas that contribute to the understanding, prevention, and management of human diseases. Contemporary health research increasingly requires multidisciplinary perspectives that bring together clinical knowledge, biological mechanisms, public health concerns, and diagnostic awareness. Within this framework, studies addressing urological conditions, women's health, and parasitic infestations offer valuable insights into different dimensions of human health.

The chapters in this volume present current discussions on selected topics in clinical and health sciences. The first chapter examines the therapeutic potential of 5α-reductase inhibition in prostatic diseases, emphasizing its relevance in the management of prostate-related disorders. The second chapter focuses on the causes of menopause among women aged 45–50 in Gombe Metropolis, Nigeria, contributing to discussions on reproductive health, women's wellbeing, and population-based health factors. The third chapter addresses human myiasis from a multidisciplinary perspective, highlighting the medical, biological, and clinical importance of dipteran infestations.

By bringing together these diverse but health-centered studies, this volume reflects the broad and interdisciplinary character of medical sciences. The chapters demonstrate how clinical research, epidemiological observation, and biological inquiry can contribute to a deeper understanding of disease processes and health-related challenges in different populations.

It is hoped that this book will serve as a useful academic resource for researchers, healthcare professionals, students, and scholars interested in clinical medicine, public health, reproductive health, parasitology, and related fields. We extend our sincere appreciation to all contributing authors for their valuable scholarly efforts.

Editorial Team
June, 2026
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CHAPTER 1
THE THERAPEUTIC POTENTIAL OF 5A-REDUCTASE INHIBITION IN PROSTATIC DISEASES

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INTRODUCTION

Androgen present in the serum and formed by leydig cells of the testes in the observation of anterior pituitary gland and hypothalamus is the testosterone. Testosterone has different kind of functions such as spermatogenesis at puberty, development of libido, muscle growth. Testosterone is converted into more potent metabolite dihydrotestosterone (DHT) by using NADPH cofactor (Figure 1).

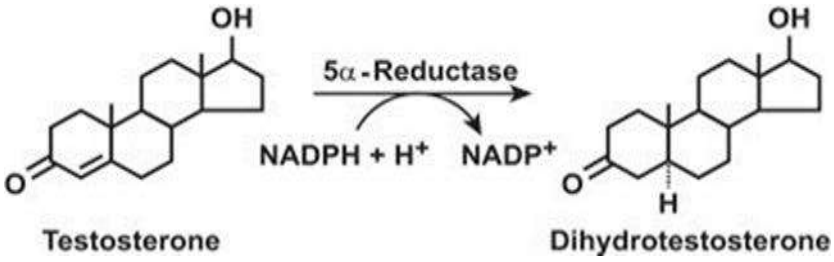


Figure 1: 5α-Reductase converting T to DHT with NADPH

Dihydrotestosterone is responsible for growth of external genitalia, prostate gland, facial and body hair. Dihydrotestosterone level in the prostatic tissue is responsible in number of human diseases like androgenic alopecia, prostate cancer, benign prostatic hyperplasia (BPH). Three isozymes of 5α-reductase encoded by SRD5A1, SRD5A2, SRD5A3. SRD5A1 is present in the periphery, SRD5A2 is present in the prostatic tissue, SRD5A3 located in the hormone refractory prostate cancer cells (HRPC) (Figure 2). SRD5A1 and SRD5A2 are present in the normal prostate tissue but overexpressed in benign prostatic hyperplasia (BPH). In Benign prostatic hyperplasia (BPH), the isozyme1 and 2 are majorly involved for hyperplasia of epithelial cells, stromal cells and finally results in the enlargement of prostate gland. At present time, drugs available for the prostatic diseases are two, that is finasteride and dutasteride, related to the 5α-reductase protein. Finasteride is the inhibitor of type 2 isozyme (SRD5A2).

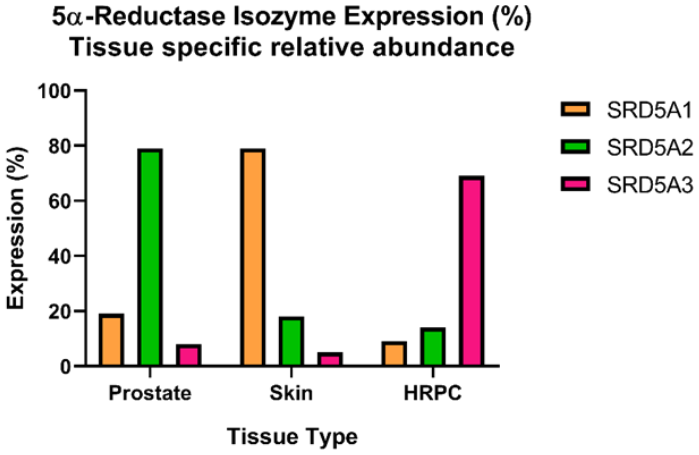


Figure 2: Relative expression of 5α-reductase isozymes across prostate tissues. Grouped bar chart showing SRD5A1/2/3 dominance in prostate (SRD5A2), skin (SRD5A1), and hormone-refractory prostate cancer (SRD5A3), highlighting therapeutic selectivity.

5α-reductase-2, steroid which is membrane embedded and belongs to 5α-reductase (SRD5A), is formed of seven trans-membrane α-helices, which are interconnected with 6 loops which are located most probably in the endoplasmic reticulum membrane. Dihydrotestosterone in the prostate cells enhances the visualisation of some particular genes; AR gene, PTEN, ETV4, Bcl-2, ETV1, are required to enhance the development and growth of prostate.

The testosterone and dihydrotestosterone level with aging is essential for function of prostate, testosterone and dihydrotestosterone level decrease with increasing age, people who are more than 50 years old [8, 9]. Males who all are suffering with benign prostatic hyperplasia (BPH) have enhanced level of dihydrotestosterone (DHT).

Benign prostatic hyperplasia is the noncancerous enlargement of the epithelial, stromal cells of prostatic gland. Benign prostatic hyperplasia is the increment of prostatic gland, block and obstruct the urinary track, due to this felling of half emptiness of urinary bladder. Approximately 50 percent pathological evidences have been collected from the males who all are above the 50 years old.

About 83 percent males by the age of 80 have disease features of benign prostatic hyperplasia (BPH), due to this BPH is considered as one major health issue nowadays. The link between serum androgens level with age and rate of risk of prostate cancer has become a major concern of research instead of benign prostatic hyperplasia (BPH), majorly in the males above the age of 40 years. Death data received 350,000 and the new cases received 1.3 million were recorded in 2018 due to prostate cancer.

Prostatectomy, the removal of prostate is helpful but due to associated risks like ejaculation problem, urinary bladder dysfunction as well as infertility, necessitates the development of alternative new treatment. Benign prostatic hyperplasia symptoms are regulated by decreasing the production of dihydrotestosterone by inhibiting the 5α-reductase-2 using the drugs like dutasteride and finasteride.

There are number of complications like infertility, after administration of finasteride and dutasteride which necessitates the development of new more potent therapeutics .

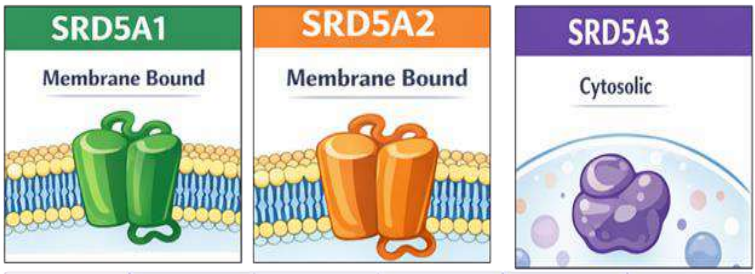
1. HISTORICAL REVIEW

5α-reductase enzyme discovery in 1954, revealed the number of diseases due to androgens such as benign prostatic hyperplasia, female hirsutism, acne, prostate cancer.5α-reductase and 5β-reductase were discovered and isolated from the rat liver homogenates. Ancient findings, it was demonstrated that 5α-reductase and 5β-reductase were required to reducing the double bond between carbons Δ4,5 of C-21, C-19 steroids. Androsterone was the first isolated androgen with 25,000 litters adult men urine. According to assumptions of the researchers until 1935, this steroid was only male hormone. Initially 5α-reductase was identified from rat liver slices, on the basis of their capability to convert deoxycorticosterone into 5α-reduced metabolites. Researchers identified the NADPH is used as a cofactor for the conversion of steroids. In the 1960s, reduction of 5α was identified as irreversible reaction, and testosterone converted into potent dihydrotestosterone in the presence of 5α-reductase in prostatic tissue. Initially 5α-reductase was identified in the slices of rat liver, due to its capability to change deoxycorticosterone to reduced metabolites of 5α.

According to their biochemical properties and location, two types of enzymes 5α-reductase1 and 5α-reductase2 have been identified. 5α-reductase1 is alkaline in pH (6-8.5) and 5α-reductase2 is acidic in pH (4.7-5.15). 5α-reductase is major enzyme required to change testosterone into dihydrotestosterone. Testosterone act as precursor of dihydrotestosterone in prostatic tissues and androgenic tissues. Dihydrotestosterone is not active in all the tissues, in the skeletal muscles very less amount of 5α-reductase, intact testosterone is used for growth, so there is no conversion of testosterone into dihydrotestosterone.

2. AMINO ACID AND CHROMOSOMAL LOCATION

5α-reductase1 contains 259AA (amino acids) and has molecular weight (MW) of 29.5 kd. 5α-reductase2 contains 254 AA and has MW of 28.4 kd. These are present in the lipid bilayer of the membrane and show very less homology of their protein sequence. 5α-reductase1 and 5α-reductase2 are present on the different chromosomes and shows the different biochemical properties. Maximum sequence homology in particular species between two isozymes is around 47% and sequence homology of same isozyme between different species 60% is 5α-reductase1 and 77% is 5α-reductase2. 5α-reductase and 5α-reductase2 genes have exons which are dislodged from one another by four introns and location of introns also same in the both the genes. SRD5A1 gene is present on chromosome 5p15 and SRD5A2 gene located on 2p23. Polymorphism of gene is present for both genes. Higher than 850 single nucleotide polymorphism (SNP) is reported for SRD5A1 and higher than 550 single nucleotide polymorphism (SNP) is reported for SRD5A2 [26]. The altered 5α-reductase2 is due to single nucleotide polymorphism in SRD5A2 gene affects the Cap risk. 5α-reductase3 contains the 318AA and shows the 19% similarity as 5α-reductase1, 20% similarity as 5α-reductase2. SRD5A3 located on the chromosome 4q12.



Isozyme	Amino Acid	Location	pH	Disease Role	Inhibitors
SRD5A1	259	Chr5p15, periphery	6-8.5	Skin disorders	Dutasteride
SRD5A2	254	Chr2p23, prostate	4.7-5.15	BPH	Finasteride
SRD5A3	318	Chr4q12, HRPC	-	Castration resistance	-

Figure 3: Functional and topological characterization of 5α-reductase isozymes

3. 5A-REDUCTASE INHIBITORS

a. 4-Azasteroids: Nitrogen atom at 4th position and 3oxo,5α-steroids are the most studied steroid such as dutasteride (GG745), finasteride (MK-906), 4-MA, MK-386 etc.

Finasteride: Finasteride is 4-azasteroid, is the 1st verified drug for the cure of BPH, male pattern baldness. Potent inhibitor, finasteride of 5α-reductase2 as compare to the 5α-reductase1. In the serum, level of dihydrotestosterone is decreased by 71%, after the 24weeks of the drug administration. In 7days administration of finasteride drug 1mg or 5mg daily, it decreases by 85% the intraprostatic dihydrotestosterone level in the men with the symptoms of lower urinary tract symptoms (LUTS) to benign prostatic enlargement. In another study 5mg/day of finasteride was given to the males with lower urinary tract symptoms to the benign prostatic enlargement.

Dutasteride: dutasteride is 4-azasteroid and is approved for half-life period of 5 weeks. only verified for the cure of benign prostatic hyperplasia (BPH). Dutasteride is dual inhibitor for 5α-reductase enzyme. It inhibits the SRD5A1 and SRD5A2 both isozymes of 5α-reductase.

In 24weeks administration of dutasteride drug, the level of dihydrotestosterone in the serum decreases fast as compare to finasteride and shows 97% decrease in intraprostatic dihydrotestosterone in men, treated with 5mg/day for 6-10 weeks.

b. 6-Azasteroids such as GIIS7669X are potent inhibitors of SRD5A1 and SRD5A2. 6-azasteroid has nitrogen at 6th position.

c. 10-Azasteroids such as AS97004, has nitrogen at 10th position and inhibits the 5α-reductase enzyme.

4. CLINICAL IMPORTANCE OF 5A-REDUCTASE

Change of testosterone (T) to dihydrotestosterone (DHT) with the help of enzyme 5α-reductase are linked with various human conditions.

4.1 Benign Prostatic Hyperplasia

BPH is non-cancerous increment of the stromal, epithelial cells of prostate gland. Enlargement of prostate gland create the obstruction of the proximal urethra and due to this problem, disturbance in the flow of urination . It is the major diseases of the elder male population and it increase with age. Every year around 0.5 million trans-urethral prostatectomies conducted world-wide and is the 2nd probable age group around 65 years old males, in which operations are performed. Benign prostatic hyperplasia is physical increment due to number of different reasons such as aging, decreased apoptosis, genetic factors, hormonal disturbance, cell growth. According to widely accepted hypothesis benign prostatic hyperplasia occurs at following aging related changes, in the prostatic androgens which are responsible for accumulation of dihydrotestosterone. Major function of dihydrotestosterone is the stimulation of the epithelial, stromal cells present in the prostate tissues, that lines the prostate gland.

Approximately 50 percent pathological evidences have been collected from the males who all are above the 50 years old. BPH is a significant public health reason, with approximately 83% of males developing the condition by the age of 80.

However, the focus of research has shifted more towards the link between serum androgen levels and the risk of prostate cancer, particularly in men over the age of 40, rather than on BPH. Prostate cancer is a major global health concern, with 1.3 million new cases over 350,000 deaths recorded worldwide in 2018. Importantly, recent large cohort studies demonstrate prediagnostic 5ARI use associates with significantly reduced prostate cancer mortality (HR 0.75, 95% CI 0.62-0.91), resolving prior concerns about high-grade disease risk while confirming chemopreventive benefits. The association between serum androgen volume and development, progression of prostate cancer has become a major area of research interest, as it may provide insights into the underlying mechanisms and potential therapeutic interventions. While the prevalence of BPH is high and it is a significant health concern, the scientific community increasingly focused its attention on understanding the nature and effect of androgens in the pathogenesis of prostate cancer, which has a substantial impact on morbidity and mortality globally. This shift in research focus reflects the growing importance of elucidating the complex relationship between androgen signaling and prostate cancer risk and progression (Figure 3).

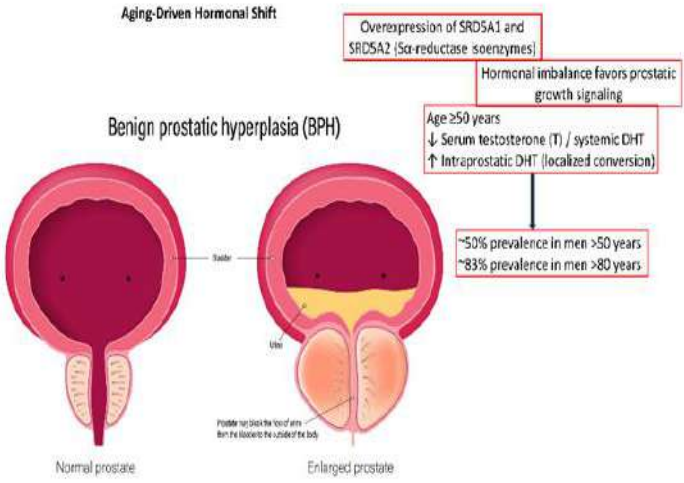


Figure 4: Aging-associated hormonal changes in Benign Prostatic Hyperplasia (BPH).

This puts to rest earlier worries regarding the danger of high-grade disease while validating the benefits of chemoprevention. Importantly, recent large cohort studies show that using 5ARI before diagnosis is linked to a much lower chance of dying from prostate cancer (HR 0.75, 95% CI 0.62–0.91). This puts to rest earlier worries regarding the danger of high-grade disease while validating the benefits of chemoprevention. Benign prostatic hyperplasia the androgen signalling increased as compare to the normal tissue. Increased androgen signalling such as dihydrotestosterone which leads to the development of benign prostatic hyperplasia pathophysiology. Reduced apoptosis accompanied by enhanced epithelial and stromal proliferation drives progressive prostate enlargement. This is further supported by upregulated growth factor signaling pathways (FGF, TGF-β, IGF) and chronic low-grade inflammation within the prostatic microenvironment. Collectively, these alterations culminate in nodular hyperplasia of prostate tissue (Figure 4). To treat the benign prostatic hyperplasia different approaches are used such as invasive therapies, surgery and drugs. Factors like age, weight, size of prostate, androgens level, and symptoms of disease are majored before specific treatment and administration.

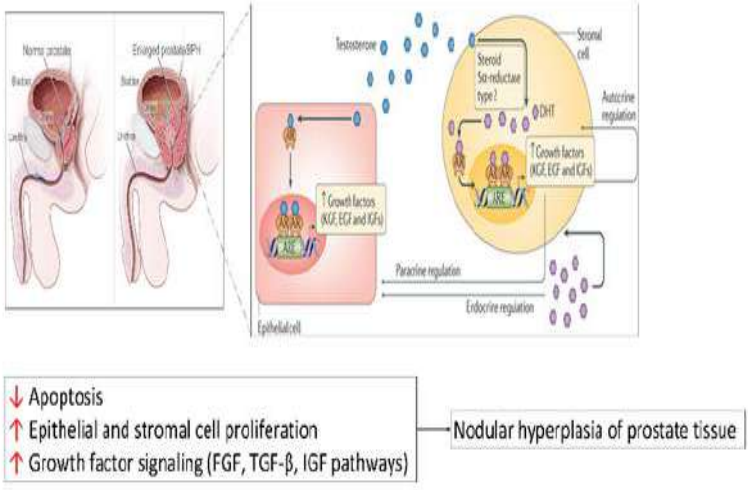


Figure 5: Cellular and molecular mechanisms driving BPH progression

4.2 5α-reductase2 Deficiency (Pseudo vaginal Peri-neo-scrotal Hypospadias)

5α-Reductase2 Deficiency (Pseudo-vaginal Perineo-scrotal Hypospadias) is a rare autosomal recessive disorder of sexual development characterized by a deficiency in the 5α-reductase 2 enzyme. This enzyme is responsible for the change of testosterone to dihydrotestosterone (DHT), a hormone crucial for male sexual differentiation. Individuals with this condition typically have female-appearing genitalia at birth, but they may exhibit virilization at puberty, such as deepening of the vocal tone, scrotal hyperpigmentation, phallus enlargement, increased muscle mass.

The diagnosis of 5α-reductase2 deficiency is often delayed due to the rarity of the condition and the potential for misdiagnosis as half or complete androgen insensitivity syndrome. Molecular testing is essential to confirm the diagnosis, which involves identifying a homozygous mutation in the SRD5A2 gene. Treatment options for 5α-reductase2 deficiency vary depending on the individual's gender identity and the severity of the condition. For those raised as females, a pro-phylactic orchiectomy, genito-plasty, estrogen therapy of substitution may be suggested. In cases where the individual chooses to transition to male, DHT/high-dose testosterone therapy can be used to increase the phallus size .

5α-Reductase2 deficiency is a genetic disorder characterized with low synthesis of dihydrotestosterone (DHT) due to mutational changes in the gene of 5α-reductase 2, leading to 46, XY sexual development disorder. Prostatic disease men born with male normal internal reproductive system but exhibit ambiguous genitalia, including a small penis, labio-scrotal fusion, and a urogenital sinus with different two urethral, vaginal openings. During onset of puberty, individuals with this condition experience a partial masculinization of their external genitalia, accompanied by increased muscle mass, phallic growth, and deepening of the voice, but their reproductive function and fertility are affected by the deficiency in DHT.

4.3 Skin Disorders due to Androgen-Stimulation (Androgenic Alopecia, Acne, Hirsutism)

Hyper-androgenism, primarily affecting females, is characterized by excessive androgen production, often caused by polycystic ovary syndrome (PCOS) or other conditions. This excess androgen is reason to increased testosterone nature in target tissues. Skin resulting in dermatological manifestations like hirsutism, acne, and androgenic alopecia. The change of testosterone to dihydrotestosterone (DHT) by 5α-reductase in skin plays a crucial role in these manifestations.

Androgens show potent action in the development of men androgenic alopecia, female pattern hair loss. During puberty, surge of androgen can decrease hair follicles, leading to male pattern baldness in individuals which are predisposed genetically. Women, androgen increment contributes to scalp hair loss, although the process differs from male pattern baldness. Hirsutism, is identified by increased coarse of growth, black dark hair in a male-like pattern on a woman's body, is typically caused by an excess of male hormones, known as androgens, in the female body. Similarly, acne is exacerbated by the surge of pubertal androgen, which show increment of sebaceous gland stimulation and sebum production in susceptible individuals. 5α-reductase enzyme nature is changed in androgen-stimulated skin disorders, such as hirsutism, scalps balding, acne-prone skin. Inhibiting this enzyme system, using drugs like finasteride and dutasteride, appears to be a promising target for treating these conditions, as it sometime result in few side effects compared to classical antiandrogens. Men with androgenic alopecia, inhibitors such as finasteride, dutasteride significantly increase hair growth increment after at least 6 months of treatment. Finasteride 1 mg every day is needed superiorly to 5% topical minoxidil in inducing hair growth, finasteride 5 mg daily is inferiorly to dutasteride 2.5mg every day in treating male androgenic alopecia. In women, neither finasteride nor dutasteride is FDA-approved for treating androgenic alopecia due to teratogenicity. The crystal structure of human steroid 5α-reductase 2 (SRD5α2) in complex with finasteride has been determined at a resolution of 2.8 Å.

This structure reveals a unique 7-transmembrane (TM) structural topology, an inter-mediate adduct of NADPH and finasteride which is a critical enzyme in metabolism of steroid that catalyses the conversion of testosterone to dihydrotestosterone. Mutational changes in the SRD5α2 gene have been associated with 5α-reductase deficiency, prostate cancer, and finasteride is a potently used anti-androgen drug for treating benign prostate hyperplasia.

SRD5α2 structure shows a large pocket inside the 7-TM domain at the cytosolic side, which is formed by every 7 TMs and loops L1, L3, L5. This pocket is completely occluded from the cytosol, with only one opening on the side of the 7-TM domain between TM1 and TM4. The electron density in the cavity reveals features of NADPH and finasteride, allowing for unambiguous modeling of both ligands. The distance between nicotinamide C4 atom of NADPH, the C2 atom of finasteride is lesser than 2 Å, helping the formation of a covalent bond.

The structure of SRD5α2 provides insights into the molecular mechanisms of enzyme catalysis of enzyme, inhibition, with the help of residues E57 and Y91. Study also suggests that the cytosolic region of SRD5α2 has high conformational dynamics, maintaining the NADPH/NADP+ exchange. Disease-causing mutations of SRD5α2 is mapped to reveal the structure and its molecular mechanisms for their pathological effects.

Finasteride exists in two crystalline polymorphic forms, form I and form II, which have different physical and chemical properties. The identification of these polymorphic forms is crucial in pharmaceutical development, as they can affect the drug's efficacy and stability. Fourier transform (FT)-Raman spectroscopy has been shown to be a useful tool for identifying the polymorphic form of finasteride in tablets, without the need for pre-treatment (Figure 6).

Biological Evaluation In Various Models

In-vitro, 5α-reductase inhibitory activity of novel compounds has been evaluated using enzyme inhibition assays (Table 1). In-vivo, the inhibitory effects on prostate weight have been assessed in animal models (Table 1). Computational in-silico models have also been used to predict the 5α-reductase inhibitory potential of new compounds as a legitimate approach for BPH drug discovery (Table 1).

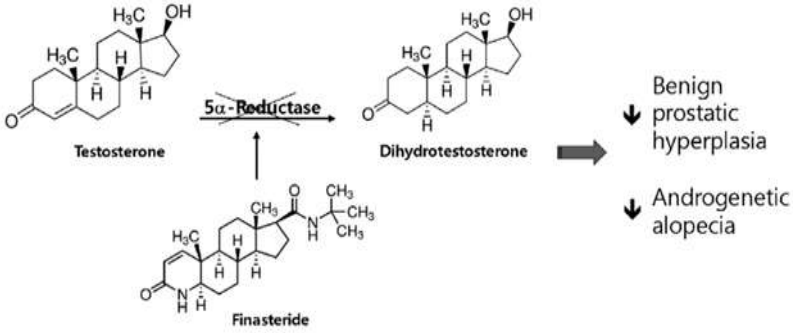


Figure 6: Mechanistic overview of Finasteride on prostatic diseases

Table 1: Biological evaluation of various 5α-reductase in-vivo and in-vitro inhibitory models and in-silico models for assessment of BPH in both humans as well as in animals.

Bio-Assay	Method	Subject/model organism	Inference
In-vivo Assay	Chicken comb method	Chicken comb	This bioassay evaluates androgenic activity by observing comb growth in newly hatched White Leghorn chicks after systemic or oral administration of test compounds. Chicks are treated daily for 7 days, then sacrificed and weighed to establish dose-response curves
In-vivo Assay	Scrotal incision method	Castrated malerats	In this method, castrated male rats receive varying doses of test compounds subcutaneously for 4 days, and their ventral prostates are analyzed for inhibition of testosterone-induced hypertrophy. The mean percentage inhibition is calculated and statistical significance between control and test groups is assessed
In-vivo Assay	Seminal vesicles test method	Castrated male hamsters	This method studies the effectiveness of test compounds on the seminal vesicles of castrated male hamsters, administering analogues for 3 days in castor oil via subcutaneous injections. Completion of treatment, after that animals sacrificed, after that seminal vesicles are weighed

Bio-Assay	Method	Subject/model organism	Inference
In-vivo Assay	Serum androgen level effective-ness	Male rats	This is the way to measures levels of circulating testosterone, DHT using radioimmunoassay/ELISA after administering proposed 5α-reductase inhibotors, indicating the compounds' inhibitory effects, which are compared with a reference drug
In-vivo Assay	Change in rat prostate weight method	Male rats	Mature male rats are orally administered a compound for 14 days to evaluate its effect on the prostate. On the 15th day, rats are anesthetized, sacrificed, and their adrenal glands, liver, ventral prostate, and seminal vesicles are removed and weighed
In-vitro Assay	Cytotoxicactivity	Prostate cancer cell lines	Cell lines of prostate cancer like DU-145, PC-3, LNCaP are used to analyze compound effects on prostate cell proliferation, investigate biochemical changes in advanced prostate cancer, evaluate chemotherapeutic responses, and develop subcutaneous tumor models in animals
MTT assay	Cytotoxic studies	Prostate cancer cell lines	MTT dye is used in cytotoxicity studies, where it is reduced from yellow to blue formazan by mitochondrial succinic dehydrogenase. The solubilized formazan from MTT reduction is measured spectrophotometrically to assess cell viability, as only metabolically active cells reduce MTT. This sensitive, easy-to-handle method is widely used for cytotoxicity testing and validated as an alternative to the Draize eye irritation test in Japan. Assay conditions and different tetrazolium dyes can affect results
In-silico studies	2D/3D QSAR	2D/3D QSAR pharmacophore models	2D/3D QSAR pharmacophore models for 5α-reductase inhibitors were generated and validated using known IC50 values. Key hydrogen bond, hydrophobic attraction with 5α-reductase identified active binding sites on the 4AT0 protein, including gatekeeper residues ALA63, THR60, and ARG456 in the hinge region

Bio-Assay	Method	Subject/model organism	Inference
In-silico studies	Molecular docking	Compound interaction with target molecule pocket	Molecular docking aids drug discovery by analyzing small molecule binding in a protein's target pocket, leveraging NMR spectroscopy and X-ray crystallography for protein sequence determination. Docking outcomes, driven by scoring functions, assess drug affinity via D-scores, adhering to Fischer's "lock-and-key" principle of geometric compatibility between ligand and receptor shapes
In-silico studies	Absorption, Distribution, Metabolism and Excretion (ADME)	ADME pharmacokinetic model	Pharmacokinetics studies, encompassing ADME processes, elucidate drug movement in the body, crucial for optimizing drug efficacy. Analyzing pharmacokinetic parameters pre-synthesis enhances drug potency and efficacy, reducing costs and failure rates while expediting development

5. DISCUSSION

The discovery of 5α-reductase enzymes in 1954 marked a significant advancement in understanding various androgen-related diseases like benign prostatic hyperplasia, female hirsutism, acne, prostate cancer. Initially isolated from rat liver homogenates, these enzymes play a crucial role in reducing the double bond between carbons Δ4,5 of C-19, C-21 steroids. Androsterone, the first isolated androgen, challenged earlier assumptions that this steroid was exclusively a male hormone. Further research revealed two distinct enzymes, 5α-reductase1 and 5α-reductase2, characterized by their biochemical properties and chromosomal locations. These enzymes, vital for converting testosterone into dihydrotestosterone, exhibit significant differences in amino acid sequence and location, with implications for their roles in androgen metabolism and related disorders. Inhibitors targeting 5α-reductase enzymes have been developed to manage conditions like benign prostatic hyperplasia, male pattern baldness. Dutasteride, finasteride prominent among these inhibitors, demonstrate potent suppression of dihydrotestosterone levels, offering therapeutic benefits in reducing prostatic enlargement and hair loss.

Other classes of inhibitors, such as 6-azasteroids and 10-azasteroids, show promise in targeting specific isoforms of 5α-reductase.

Clinically, 5α-reductase shows a pivotal effect in various disorders such as benign prostatic hyperplasia, 5α-reductase2 deficiency, which manifests as pseudo vaginal peri-neo-scrotal hypospadias. Moreover, dysregulation of androgen metabolism contributes to androgen-stimulated skin disorders like androgenic alopecia, acne, hirsutism, where inhibition of 5α-reductase emerges as a therapeutic strategy to mitigate symptoms. The structural and functional analysis of 5α-reductase, provides valuable insights for drug development. The SRD5α2 crystal structure in combination with finasteride provides critical direction for the activity of steroid reductases of integral membrane and also will help in drug development. The study of finasteride polymorphs is essential for understanding its properties and behavior in pharmaceutical formulations.

CONCLUSION

The prevalence of benign prostatic hyperplasia (BPH), a situation that impedes the quality of life in older men, is show enhancement at an alarming rate. Unfortunately, the current chemotherapeutic options for BPH are limited, expensive, associated with concerning toxicity effects. Moreover, there is an urgent need for the drug discovery community to identify more potent 5α-reductase inhibitors that can effectively manage BPH. While 5α-reductase inhibitors are considered promising therapeutic agents, they all have significant drawbacks that have hindered their widespread clinical adoption. An alternative approach that could prove fruitful is the repurposing of existing medications that have already demonstrated safety and efficacy in clinical trials. This strategy could potentially provide new therapeutic interventions for BPH without the need for extensive de novo drug development. However, the growing prevalence of BPH, coupled with the limitations of current treatments, underscores the critical need for the identification and development of more effective and well-tolerated 5α-reductase inhibitors. Repurposing existing drugs may offer a viable path forward to address this unmet medical need.

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CHAPTER 2
CAUSES OF MENOPAUSE AMONG WOMEN AGED 45-50 IN GOMBE METROPOLIS,GOMBESTATE, NIGERIA

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INTRODUCTION

Women are biologically at risk of health complications. These include puberty, pregnancy, breastfeeding, and menopause, which require women to be more attentive to their health (Modoodi et al., 2020). Epidemiological studies have shown that 65-85% of women experience menopausal complications (Diyu & Satriani, 2022). Menopause is a biological condition where menstruation stops in a woman due to the failure of the follicular actions of the ovaries. It is a stage when the menstrual cycle stops for longer than 12 months and there is a drop in the levels of estrogen and progesterone, the two most important hormones in the female body (WHO, 2020). The onset of this physiological development not only marks the end of women's reproductive function but also introduces them to a new phase of life (Diyu, & Satriani, 2022).

Even though, it is a phenomenal occurrence among women. It varies from one woman to another due to diffences of age and manifesting signs. there is a considerable variation wwomen regarding the age of attaining menopause and the manifestation of menopausal signs and symptoms. Worldwide, the estimates for the median age at menopause range from 45 to 55 years with women from Western countries having a higher menopausal age compared to women from other parts of the world (Sumeyye and Ummuhan, 2021).

The causal factor of earlier menopause remains elusive. Although several genes identified play roles particularly in the development of premature menopause (Hoyos et al., 2019), they cannot explain majority of cases (Seung and Joohon, 2020). Environmental and behavioral factors, such as obesity, ethnicity (African-American or Hispanic ancestry), early onset of smoking, higher parity, and lower socioeconomic status, are also associated with early menopause (Hewlett and Mahalingaiah, 2021). Early menarche is associated with earlier menopause in several studies (Zsakai et al., 2019). Studies have linked nulliparity and socioeconomic factors for menopause in Europe and India were found to. This heterogeneity in the effect of biologic and social factors on age at menopause across ethnicities, cultural context, or data source may contribute to general incidence of premature or early menopause (Seung and Joohon, 2020).

Additionally, medical conditions like premature ovarian failure (POF), polycystic ovary syndrome (PCOS), and thyroid disorders can also contribute to early menopause (ACOG, 2020). This process can also be induced by surgery or medical treatment, leading to a sudden and abrupt onset of menopause.

The perimenopause can start many years before it reaches the final stage and is characterized by hormonal fluctuations causing many signs such as hot flashes, night sweats, mood swings, sleep disturbances, and vaginal dryness. These symptoms can range from mild to severe and can significantly impact a woman's quality of life (Diyu & Satriani, 2022).

The physiological changes during menopause begins with the failure of follicular activity in the ovaries. This hormonal decline not only ends a woman's reproductive function but also introduces a new phase of life with unique health considerations. For example, the reduction in estrogen levels is associated with increased risks of osteoporosis, cardiovascular disease, and urogenital atrophy (Thurston et al., 2020).

Globally, menopause is experienced by all women, but the age of onset and the prevalence of symptoms can differ. In Nigeria, the average age of menopause is reported to be slightly lower than the global average, typically ranging between 47 and 49 years (Okonofua, et al., 2020). The prevalence of early menopause varies across regions, with studies reporting rates ranging from 22.2% in Lagos (Okeke, 2019) to 27.1% in Kano (Iliyasu, 2020). These variations are influenced by factors such as genetics, nutrition, and socio-economic conditions. Understanding the causes of early menopause, knowledge levels about menopause, its impact on the physical and emotional well-being of women and exploring the socio-cultural perceptions and stigmas associated with menopause in Gombe State, is crucial for developing targeted interventions to improve women's health outcomes. This study centrally focused on the causes, impacts and ways of addressing the challenges of menopause among women in Gombe metropolis, Gombe state, Nigeria.

Concept of Menopause

Menopause is a medical condition that marks the end of a woman's reproductive years. It is typically characterized by the cessation of menstruation, usually occurring between the ages of 45 and 55. The onset of menopause could have significant implications for women's health, impacting various aspects of their physical and emotional well-being. Menopause is defined as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity. The transitional phase leading up to menopause, known as perimenopause, is characterized by irregular menstrual cycles and fluctuating hormone levels. The decline in ovarian function is central to menopause, leading to reduced levels of estrogen and progesterone. This hormonal change is associated with various physiological and psychological symptoms, including hot flashes, night sweats, and mood swings.

Stages of Menopause

Perimenopause

Perimenopause is the transitional period leading up to menopause, typically beginning in a woman's 40s, although it can start as early as the mid-30s. This phase is marked by a gradual decline in ovarian function, resulting in fluctuating hormone levels, particularly estrogen and progesterone. These hormonal changes lead to a range of symptoms, such as irregular menstrual cycles, hot flashes, night sweats, mood swings, and sleep disturbances. Research shows that the length of perimenopause can vary widely among women, lasting anywhere from a few months to several years. The variability in symptoms and their severity during this stage is influenced by factors such as genetics, lifestyle, and overall health. The decline in estrogen during perimenopause is particularly significant because estrogen plays a critical role in many bodily functions beyond reproduction, including maintaining bone density and regulating cardiovascular health. As estrogen levels fluctuate, women may experience symptoms that affect their quality of life and require medical intervention. Recent studies suggest that lifestyle modifications, such as regular exercise and a balanced diet, can help manage the symptoms of perimenopause and reduce the risk of chronic conditions associated with this stage.

Hormone replacement therapy (HRT) is also commonly recommended for managing more severe symptoms, although it is important to consider the potential risks and benefits.

Menopause

Menopause is defined as the point in time when a woman has not experienced a menstrual period for 12 consecutive months, marking the end of her reproductive years. This stage is a natural biological process that typically occurs between the ages of 45 and 55, with the average age being 51. The onset of menopause is confirmed by the permanent cessation of ovarian function, which leads to a significant decrease in the production of estrogen and progesterone. The hormonal changes during menopause can trigger various symptoms, including hot flashes, vaginal dryness, and emotional changes, which can vary in intensity from woman to woman. The transition to menopause is influenced by several factors, including genetics, lifestyle, and environmental factors. For instance, women who smoke tend to reach menopause earlier than non-smokers, while factors such as higher body mass index (BMI) and the use of oral contraceptives are associated with a later onset. The decline in estrogen levels during menopause also increases the risk of developing chronic conditions such as osteoporosis, cardiovascular disease, and type 2 diabetes. Understanding the timing and implications of menopause is crucial for managing its symptoms and mitigating the associated health risks.

Causes of Menopause

Age-Related Factors

The natural aging process is a critical determinant of menopause, primarily due to the depletion of ovarian follicles, which are responsible for the production of eggs and the regulation of menstrual cycles. As women age, the number of functioning ovarian follicles decreases, leading to reduced levels of estrogen and progesterone, the hormones crucial for reproductive health. This decline in hormone production triggers the onset of menopause, typically marked by the cessation of menstruation after 12 consecutive months without a period.

The biological clock is often set at birth, with a fixed number of ovarian follicles that progressively diminish throughout a woman's life, culminating in menopause. Global studies have shown that the average age of menopause onset is around 51 years, although this can vary significantly depending on genetic, environmental, and lifestyle factors. For instance, lifestyle factors such as smoking, diet, and overall health can influence the timing of menopause. Smoking has been consistently associated with an earlier onset of menopause, likely due to its impact on ovarian function. Conversely, higher body mass index (BMI) and prolonged use of hormonal contraceptives may delay menopause. These findings suggest that while aging is the primary driver of menopause, individual lifestyle choices and environmental factors can modify its timing.

Genetic Factors

Genetic predisposition plays a significant role in determining the age at which menopause occurs. Research indicates that the timing of menopause is heritable, with familial patterns observed in the onset age among close relatives. Women with a family history of early menopause are more likely to experience it themselves, suggesting that specific genetic factors are at play. Genome-wide association studies (GWAS) have identified several genetic loci associated with the age at natural menopause, highlighting the complex genetic architecture underlying this process. In addition to specific gene variants, epigenetic factors—changes in gene expression that do not involve alterations to the underlying DNA sequence—may also influence the timing of menopause. For example, genetic mutations in genes involved in DNA repair, such as BRCA1 and BRCA2, have been linked to an earlier onset of menopause. Furthermore, variations in the FMR1 gene, associated with Fragile X syndrome, have been linked to both premature ovarian insufficiency and early menopause. These genetic insights not only help to predict the timing of menopause but also provide potential targets for interventions aimed at delaying its onset or managing its symptoms.

Lifestyle Factors

Smoking

Smoking is one of the most significant lifestyle factors associated with an earlier onset of menopause. Research indicates that women who smoke are more likely to experience menopause up to two years earlier than non-smokers. This is primarily due to the harmful effects of nicotine and other toxins found in cigarettes, which accelerate the depletion of ovarian follicles. These toxins increase oxidative stress and cause direct damage to the ovarian tissue, leading to reduced estrogen production and premature ovarian aging. Additionally, smoking has been shown to disrupt the endocrine system, further exacerbating the decline in reproductive hormones. The impact of smoking on menopause is dose-dependent, meaning that the more a woman smokes, the earlier she is likely to enter menopause. This is particularly concerning given that early menopause is associated with a higher risk of cardiovascular disease, osteoporosis, and all-cause mortality. Smoking cessation, therefore, is crucial not only for general health but also for delaying the onset of menopause and reducing the associated health risks. Public health interventions that promote smoking cessation among women can play a significant role in mitigating the adverse effects of early menopause.

Diet and Physical Activity

A balanced diet and regular physical activity are essential for maintaining overall health and can also influence the timing of menopause. Studies have shown that women who consume a diet rich in fruits, vegetables, and whole grains tend to experience menopause later than those with less nutritious diets. These foods are high in antioxidants and phytoestrogens, which help to regulate hormone levels and protect ovarian function. In contrast, diets high in processed foods, saturated fats, and sugars have been linked to earlier menopause, likely due to their negative impact on metabolic and cardiovascular health. Physical activity also plays a crucial role in delaying menopause. Regular exercise helps to maintain a healthy body weight, reduce inflammation, and improve cardiovascular health, all of which are important for hormonal balance and reproductive health.

Women who engage in moderate to vigorous physical activity are less likely to experience early menopause and are more likely to enjoy a healthier postmenopausal life. The benefits of exercise extend beyond delaying menopause to include a reduced risk of osteoporosis, cardiovascular disease, and other chronic conditions associated with aging.

Health Conditions and Medical Interventions

Autoimmune Diseases

Autoimmune diseases, such as lupus and rheumatoid arthritis, can lead to premature ovarian failure, resulting in early menopause. In these conditions, the immune system mistakenly attacks the body's own tissues, including the ovaries, leading to inflammation and damage that impairs ovarian function. This autoimmune response can reduce the number of viable ovarian follicles, leading to a decrease in estrogen production and an earlier onset of menopause. The risk of early menopause is particularly high in women with autoimmune disorders who require aggressive treatments, such as immunosuppressive drugs, which can further affect ovarian function. The impact of autoimmune diseases on menopause highlights the importance of early diagnosis and management of these conditions to preserve reproductive health. In some cases, fertility preservation techniques, such as egg freezing, may be recommended for women with autoimmune disorders who wish to delay childbearing and mitigate the risk of early menopause. Ongoing research is exploring the role of immunomodulatory therapies in protecting ovarian function and delaying menopause in women with autoimmune diseases.

Chemotherapy and Radiation Therapy

Chemotherapy and radiation therapy, commonly used to treat cancer, can have significant effects on ovarian function, often leading to early menopause. These treatments target rapidly dividing cells, which include not only cancer cells but also the cells in the ovaries responsible for producing eggs and hormones. The extent of the damage to the ovaries depends on the type and dose of chemotherapy or radiation, as well as the woman's age at the time of treatment. Younger women may experience a temporary cessation of menstruation, known as chemotherapy-induced amenorrhea, which can

sometimes be reversible, while older women are more likely to experience permanent menopause. The risk of early menopause is a significant concern for cancer survivors, particularly those who have not yet completed their families. Fertility preservation strategies, such as egg or embryo freezing, should be discussed with women of reproductive age before undergoing cancer treatment. Additionally, the use of gonadotropin-releasing hormone (GnRH) analogs during chemotherapy has been shown to protect ovarian function and reduce the risk of early menopause in some cases. Post-treatment, women who experience early menopause may require hormone replacement therapy to manag

Environmental Factors

Exposure to Environmental Toxins

Environmental toxins, including chemicals such as phthalates, bisphenol A (BPA), and heavy metals, have been implicated in the earlier onset of menopause. Phthalates, commonly found in plastics, cosmetics, and household products, can act as endocrine disruptors, interfering with hormone production and function. These chemicals can accelerate ovarian aging by inducing oxidative stress and damaging the DNA in ovarian cells, leading to reduced ovarian reserve and earlier menopause. Studies have also shown that women with higher levels of phthalates in their bodies tend to experience menopause several years earlier than those with lower levels. The pervasive nature of these environmental toxins poses a significant public health challenge, as they are difficult to avoid entirely. However, reducing exposure by choosing phthalate-free products, avoiding plastics for food storage, and minimizing the use of personal care products with harmful chemicals can help mitigate the risk. Continued research is needed to better understand the long-term effects of environmental toxins on reproductive health and to develop strategies for reducing exposure and protecting ovarian function.

Socioeconomic Status

Socioeconomic status (SES) is another important factor influencing the timing of menopause. Women with lower SES are more likely to experience early menopause, a phenomenon likely driven by a combination of stress, poor nutrition, and limited access to healthcare. Chronic stress, often associated with financial instability and social disadvantage, can disrupt the hypothalamic-pituitary-ovarian axis, leading to hormonal imbalances and earlier depletion of ovarian follicles. Additionally, poor nutrition, which is more common in lower SES populations, can contribute to earlier menopause by accelerating the decline in ovarian function. Access to healthcare also plays a crucial role in determining the age of menopause. Women with limited access to healthcare are less likely to receive timely interventions for conditions that could impact reproductive health, such as obesity, diabetes, and hypertension. They are also less likely to receive information on lifestyle modifications that could delay menopause, such as smoking cessation, healthy diet, and regular exercise. Addressing these socioeconomic disparities is essential for improving reproductive health outcomes and ensuring that all women have the opportunity to experience menopause at the appropriate age for their individual biology.

Psychological and Emotional Impact

Menopause is a significant life transition that often brings profound psychological and emotional changes. The hormonal fluctuations associated with menopause, particularly the decline in estrogen, are closely linked to increased vulnerability to mood disorders. Research indicates that women in the menopausal transition are at a higher risk of developing anxiety, depression, and mood swings compared to premenopausal women. These mood disturbances are not just the result of biological changes but are also influenced by the broader psychosocial context in which menopause occurs. For instance, women may experience feelings of loss related to their reproductive capacity, changes in body image, and concerns about aging, all of which can contribute to emotional distress. The severity and nature of psychological symptoms during menopause can vary widely among women. Some may experience mild, transient symptoms, while others face more severe, chronic issues that significantly impact their quality of life (Henderson et al., 2020).

Additionally, the experience of menopause can exacerbate pre-existing mental health conditions. For example, women with a history of depression are more likely to experience a recurrence of depressive symptoms during menopause (Freeman et al., 2021). The interplay between hormonal changes and psychological well-being underscores the need for comprehensive care that addresses both the physical and emotional aspects of menopause (Bromberger & Kravitz, 2020).

Coping mechanisms are crucial in managing the psychological impact of menopause. Social support is one of the most effective buffers against the negative emotional effects of menopause. Women who maintain strong relationships with family, friends, and community networks tend to report lower levels of anxiety and depression during this period (Oluwaseun & Adeyemi, 2022). Support groups, whether in-person or online, provide a space for women to share their experiences and strategies for coping with menopausal symptoms, which can reduce feelings of isolation and increase emotional resilience (Hunter & Rendall, 2021).

Mental health services also play a critical role in addressing the psychological impact of menopause. Therapeutic interventions, such as cognitive-behavioral therapy (CBT), have been shown to be effective in alleviating menopausal symptoms like anxiety and depression (Avis et al., 2020). CBT helps women develop coping strategies to manage negative thoughts and emotions, improving their overall mental health and quality of life during menopause. Additionally, mindfulness-based stress reduction (MBSR) techniques have gained popularity as a way to manage menopausal symptoms by promoting relaxation and emotional regulation (Grossman et al., 2021).

Given the complex and multifaceted nature of the psychological impact of menopause, a multidisciplinary approach that includes both medical and psychological support is essential for improving outcomes for women undergoing this life transition (Sherman et al., 2021).

1. THEORETICAL FRAMEWORK

Biological Aging Theory

The Biological Aging Theory, proposed by Jean Martin Charcot (1890s) and later expanded by Smith & Lee (2023), posits that menopause is primarily a result of the natural aging process. As women age, the number of ovarian follicles declines, leading to decreased production of estrogen and reproductive hormones Menopause occurs when the ovaries no longer release eggs regularly and estrogen levels drop significantly. In Gombe, aging is considered a significant determinant of menopause onset, with factors such as genetics, health status, and nutrition playing crucial roles.

Critique: While this theory explains menopause as a universal biological process, it does not account for variations in the age of onset across different populations. Studies indicate that factors such as malnutrition, environmental stressors, and health access can accelerate menopause (Garcia et al., 2020), highlighting the need for an integrated perspective.

Endocrine Theory

The Endocrine Theory, developed by Guillemin and Schally (1977) and further explored by Evans and Taylor (2022), relates menopause to hormonal regulatory changes. According to this theory, menopause results from the decline of the hypothalamic-pituitary-ovarian axis, leading to reduced levels of sex hormones, particularly estrogen and progesterone. These hormonal imbalances trigger the physiological changes associated with menopause.Critique: Although the Endocrine Theory effectively addresses the hormonal mechanisms of menopause, it overlooks external influences such as lifestyle choices, environmental factors, and psychological stressors. Research shows that behaviors like smoking and sedentary lifestyles can lead to early menopause (Chen et al., 2021).

Psychosocial Stress Theory

The Psychosocial Stress Theory, introduced by Lupien et al. (2009), suggests that stressors including economic hardship, societal expectations, and familial responsibilities can affect the timing and experience of menopause.

Women in Gombe face various socio-economic challenges, including poverty and limited access to healthcare, which may contribute to earlier or more severe menopausal symptoms.Critique: This theory highlights the influence of social and economic stress on menopause but lacks a biological basis. Moreover, it does not consider how individual resilience and support systems might mitigate stress-related effects on menopause.

Socio-Cultural Theory

The Socio-Cultural Theory, advanced by Margaret Lock (1993) and further supported by Williams (2022), examines how cultural norms and societal expectations shape menopause experiences. In many African societies, women's roles are tied to their reproductive capabilities, and menopause may be perceived as a loss of identity or purpose. Cultural beliefs about aging and fertility influence how women perceive and cope with menopause.Critique: While this theory underscores the importance of cultural context, it overlooks individual differences. Some women may view menopause positively, experiencing empowerment rather than loss, which the theory does not fully address.

Integration of the Theories

A comprehensive understanding of menopause requires integrating biological, hormonal, psychological, and socio-cultural factors. The Biological Aging Theory explains the natural aging process leading to menopause, while the Endocrine Theory details the hormonal changes that trigger menopause symptoms. The Psychosocial Stress Theory highlights external stressors that can influence menopause onset, and the Socio-Cultural Theory provides insights into how societal norms shape women's experiences of menopause.For this study on the causes of menopause among women in Gombe State, the Psychosocial Stress Theory is the most relevant theory. This is because socio-economic factors such as poverty, limited healthcare access, and cultural expectations are significant contributors to early menopause in the region. While biological and hormonal factors are inherent, the unique stressors faced by women in Gombe play a crucial role in the onset and experience of menopause.

Therefore, the study will adopt the Psychosocial Stress Theory as its guiding framework, examining how socio-economic and environmental factors influence menopause among women in Billiri Local Government, Gombe State.

2. METHODOLOGY

The study adopted a descriptive design.The design was found appropriate for this study as it allowed for the systematic collection, analyses and interpretation of data on menopause in Gombe metropolis. The population of the study consisted of women around 45 to 50 years who were expectedly to began menopausal characteristics. The sample size was put at 100 women and they were determined based on the purposive sampling technique. They were selected based on their knowledge of the topic under review.In this study, a quantitative approach were used to gathered the data using structured questionnaires. The questionnaire were designed to gather statistical information regarding respondents' experiences with menopause. The questionnaire consisted of closed-ended questions that allowed for easy quantification and analysis of the data.The analyses of the collected data were conducted with the aid of Special Package for Social Sciences (SPSS) where the data were presented in descriptive statistics such as the frequency and percentages which facilitated the presentation of the prevalence of menopause in Gombe metropolis, Gombe State. The adoption of descriptive statistics, particularly frequency and percentage analyses, were justified based on the need for a clear and comprehensive presentation of the prevalence of menopause in Gombe State.

3. RESULTS OF THE FINDINGS

Table 1. Socio-Demographic Characteristics of Respondents

Socio-Demographic Characteristics	Frequency	Percentage (%)
Age		
45-50	37	37.0
51-60	31	31.0
61-65	13	13.0
66-70	12	12.0
71-75	5	5.0
76-80	2	2.0
Total	100	100.0
Marital Status		
Single	11	11.0
Married	59	59.0
Divorced	11	11.0
Widowed	19	19.0
Total	100	100.0
Educational Level		
No formal education	22	22.0
Primary education	13	13.0
Secondary education	22	22.0
Tertiary education	43	43.0
Total	100	100.0
Occupation		
Unemployed	33	33.0
Self-employed	33	33.0
Civil servant	24	24.0
Others	10	10.0
Total	100	100.0

Table 1 presents the demographic information of the respondents. The age distribution shows a predominantly middle-aged group, with the largest number (37.0%) in the 45-50 age range, followed by 31 respondents (31.0%) in the 51-60 range. Smaller percentages are seen in the older age groups, with only 2 respondents (2.0%) in the 76-80 age range.

In terms of marital status, the majority of respondents were married (59.0%), with 19 respondents (19.0%) being widowed. Equal numbers of respondents are single and divorced (11.0% each).For educational background, 43.0% of respondents have tertiary education, with 22.0% having no formal education and an equal number (22.0%) having secondary education. The smallest group holds primary education qualifications, at 13.0%.Regarding occupation, the largest groups are either unemployed or self-employed, each accounting for 33.0% of the sample. Civil servants make up 24.0%, while 10.0% of respondents fall into the "Others" category.

Overall, the sample includes a diverse mix of age groups, marital Statuses, educational levels, and occupational Statuses, with a strong representation of middle-aged, married, and self-employed individuals. This demographic data provides a solid foundation for understanding the socio-economic context of the respondents in relation to the study.

Table 2. Whether menopause is primarily caused by hormonal changes

Optional Responses	Frequency	Percentage
Strongly Agree	56	56.0%
Agree	42	42.0%
Uncertain	1	1.0%
Strongly Disagree	1	1.0%
Total	100	100.0%

Table 2 illustrates the respondents' views on the primary cause of menopause. The majority of respondents, 56 (56.0%), strongly agree that menopause is primarily caused by hormonal changes, while 42 respondents (42.0%) agree with this statement. This reflects a clear consensus, with 98.0% of respondents acknowledging hormonal changes as a primary factor in menopause.

Only 1 respondent (1.0%) was uncertain, and an additional 1 respondent (1.0%) strongly disagreed. Overall, the results indicates strong agreement on the role of hormonal changes in menopause.

Table 3. Whether genetics play a significant role in determining the onset of menopause

Optional Responses	Frequency	Percentage
Strongly Agree	40	40.0%
Agree	54	54.0%
Uncertain	1	1.0%
Disagree	2	2.0%
Strongly Disagree	3	3.0%
Total	100	100.0%

Table 3 presents the responses regarding the role of genetics in determining the onset of menopause. A large majority of respondents, 54 (54.0%) agree, and 40 respondents (40.0%) strongly agree that genetics play a significant role in the onset of menopause. This reflects a strong belief in the genetic influence, with a cumulative 94.0% supporting the view. However, 5 respondants (5.0%) were either uncertain, disagree, or strongly disagreed, suggesting some variation in opinions, but genetics is still widely regarded as an important factor.

Table 4. Whether lifestyle factors such as diet and exercise affect the onset of menopause

Optional Responses	Frequency	Percentage
Strongly Agree	12	12.0%
Agree	18	18.0%
Uncertain	45	45.0%
Disagree	22	22.0%
Strongly Disagree	3	3.0%
Total	100	100.0%

Table 4 reflects the respondents' views on the impact of lifestyle factors, such as diet and exercise, on the onset of menopause. A small portion, 12 (12.0%) strongly agree, and 18 respondents (18.0%) agree with the idea that lifestyle factors affect menopause onset.

However, a large number of respondents, 45 (45.0%), are uncertain about this influence, and 22 respondents (22.0%) disagree, while 3 (3.0%) strongly disagree. The significant uncertainty and disagreement suggest that there is no strong consensus on this topic, lifestyle factors are seen as less decisive by many.

Table 5. Whether chronic illnesses like diabetes and hypertension contribute to early menopause

Optional Responses	Frequency	Percentage
Strongly Agree	24	24.0%
Agree	52	52.0%
Uncertain	14	14.0%
Disagree	9	9.0%
Strongly Disagree	1	1.0%
Total	100	100.0%

Table 5 illustrates the respondents' opinions on whether chronic illnesses like diabetes and hypertension contribute to early menopause. A majority, 52 (52.0%) agree, and 24 respondents (24.0%) strongly agree with this statement, suggesting a strong belief in the impact of chronic illnesses on menopause timing. However, 14 respondants (14.0%) were uncertain, and a small portion, 9 (9.0%), disagreed, with 1 respondant (1.0%) strongly disagreeing. Overall, the data suggest that chronic illnesses are largely seen as contributing to early menopause, though some respondants remain uncertain.

Table 6. Whether socioeconomic factors influence the age at which menopause begins

Optional Responses	Frequency	Percentage
Strongly Agree	10	10.0%
Agree	16	16.0%
Uncertain	17	17.0%
Disagree	34	34.0%
Strongly Disagree	23	23.0%
Total	100	100.0%

Table 6 shows the responses on whether socioeconomic factors influence the age at which menopause begins.

A smaller proportion of respondents, 10 (10.0%), strongly agree, and 16 respondents (16.0%) agree with this idea. In contrast, a significant number, 34 respondents (34.0%), disagree, and 23 (23.0%) strongly disagree, reflecting a large skepticism about the influence of socio-economic factors on the onset of menopause. The data suggest that while a portion of Respondents sees socio-economic factors as influential, the majority disagree with this view.

Table 7. Exposure to environmental toxins can lead to premature menopause

Optional Responses	Frequency	Percentage
Strongly Agree	7	7.0%
Agree	25	25.0%
Uncertain	34	34.0%
Disagree	32	32.0%
Strongly Disagree	2	2.0%
Total	100	100.0%

Table 7 presents the respondents' views on the impact of environmental toxins on the onset of premature menopause. A significant portion, 25 (25.0%) agree, and 7 respondents (7.0%) strongly agree with the idea that exposure to environmental toxins can lead to premature menopause. However, 34 respondents (34.0%) were uncertain, and a larger portion, 32 (32.0%) disagreed, with 2 respondants (2.0%) strongly disagreeing. This indicates a divide in options, with a moderate number of Respondents remaining unsure or dismissing the idea of environmental toxins playing a significant role.

Table 8. Whether high levels of stress accelerate the onset of menopause

Optional Responses	Frequency	Percentage
Strongly Agree	28	28.0%
Agree	59	59.0%
Uncertain	8	8.0%
Disagree	5	5.0%
Total	100	100.0%

Table 8 highlights respondents' views on the impact of stress on the onset of menopause. A large majority, 59 (59.0%) agree, and 28 respondents (28.0%) strongly agree that high levels of stress accelerate the onset of menopause.

Only a small portion, 8 respondants (8.0%), were uncertain, and just 5 respondants (5.0%) disagreed with this statement. The majority of Respondents believe that stress plays a significant role in accelerating menopause, showing a strong consensus on the topic.

Table 9. Whether menopause significantly affects women's mental health

Optional Responses	Frequency	Percentage
Strongly Agree	36	36.0%
Agree	54	54.0%
Uncertain	5	5.0%
Disagree	3	3.0%
Strongly Disagree	2	2.0%
Total	100	100.0%

Table 9 shows that the majority of respondents, 54 (54.0%) agree, and 36 respondents (36.0%) strongly agree that menopause significantly affects women's mental health. This cumulative 90.0% indicates a strong perception that menopause has a mental health impact. A small number of Respondents, 5 (5.0%), were uncertain, and just 4 respondents (4.0%) disagree or strongly disagreed. This suggests that menopause's mental health implications are widely recognized among the respondents.

Table 10. Whether physical symptoms of menopause, including hot flashes and fatigue, disrupt daily life

Optional Responses	Frequency	Percentage
Strongly Agree	34	34.0%
Agree	58	58.0%
Uncertain	6	6.0%
Disagree	2	2.0%
Total	100	100.0%

Table 10 presents the opinions of the respondents where (58.0%) agree that signs such as hot flashes and fatigue can disrupt daily life. This indicates a strong consensus that menopause has a considerable effect on daily activities.

A small group, 6 Respondents (6.0%), were uncertain, and only 2 respondants (2.0%) disagreed. The results suggest that the physical symptoms of menopause are widely acknowledged as disruptive to everyday life.

Table 11. Whether menopause reduces productivity among women in the workplace

Optional Responses	Frequency	Percentage
Strongly Agree	16	16.0%
Agree	28	28.0%
Uncertain	27	27.0%
Disagree	26	26.0%
Strongly Disagree	3	3.0%
Total	100	100.0%

Table 11 shows the effect of menopause on women's productivity in the workplace. A combined 44% (16 strongly agree and 28 agree) believe that menopause reduces productivity. However, 27.0% of the responses indicates uncertain opinions, and 28.0%) disagreed, with 2.0% strongly disagreed. This indicates a moderate division in opinions, with many respondents acknowledging some effect on productivity but others skeptical or uncertain about its significance.

Table 12. Whether menopause affects relationships with family and friends

Optional Responses	Frequency	Percentage
Strongly Agree	13	13.0%
Agree	22	22.0%
Uncertain	39	39.0%
Disagree	24	24.0%
Strongly Disagree	2	2.0%
Total	100	100.0%

Table 12 reflects the opinions of the respondents on the effect of menopause on relationships with family and friends. Only 13.0% strongly agree, and 22.0% respondents agree that menopause affects these relationships. However, 39 respondents (39.0%) were uncertain, and 26 respondants (26.0%) disagreed, with 2 respondants (2.0%) strongly disagreeing.

The uncertainty and disagreement suggest that while some see menopause as affecting relationships, many others do not perceive it as a significant factor in this area.

Table 13. Whether menopause increases health risks

Optional Responses	Frequency	Percentage
Strongly Agree	21	21.0%
Agree	66	66.0%
Uncertain	9	9.0%
Disagree	4	4.0%
Total	100	100.0%

Table 13 above shows respondents' views on whether menopause increases health risks. It reveals that 21.0% of respondents strongly agree, 66.0% of respondents agree, 9 respondents (9.0%) are uncertain, and 4.0% of respondents disagree. The majority of Respondents (87.0%) agree that menopause increases health risks, indicating widespread awareness of potential health impacts.

Table 14. Whether sleep disturbances during menopause reduce overall well-being

Optional Responses	Frequency	Percentage
Strongly Agree	13	13.0%
Agree	39	39.0%
Uncertain	39	39.0%
Disagree	8	8.0%
Strongly Disagree	1	1.0%
Total	100	100.0%

Table 14 above present respondents' views on whether sleep disturbances during menopause reduce overall well-being. It shows that 13 respondants (13.0%) strongly agree, 39 respondants (39.0%) agree, 39 respondants (39.0%) are uncertain, 8 respondants (8.0%) disagree, and 1 respondant (1.0%) strongly disagree. While 52.0% of Respondents agree, a significant portion (39.0%) remains uncertain, indicating a mixed perception of the impact of sleep disturbances.

Table 15. Whether menopause can lead to financial strain due to increased Healthcare needs

Optional Responses	Frequency	Percentage
Strongly Agree	25	25.0%
Agree	56	56.0%
Uncertain	15	15.0%
Disagree	3	3.0%
Strongly Disagree	1	1.0%
Total	100	100.0%

Table 15 above demonstrates respondents' views on whether menopause can lead to financial strain due to increased Healthcare needs. It reveals that 25 respondents (25.0%) strongly agree, 56 respondants (56.0%) agree, 15 respondants (15.0%) are uncertain, 3 respondants (3.0%) disagree. The majority of Respondents (81.0%) agree that menopause can lead to financial strain, reflecting significant concern about the financial challenges linked to healthcare during menopause.

Table 16. Whether counseling services should be provided to help Women prepare for Menopause

Optional Responses	Frequency	Percentage
Strongly Agree	51	51.0%
Agree	44	44.0%
Uncertain	1	1.0%
Disagree	4	4.0%
Total	100	100.%

Table 16 above reveals respondents' views on whether counseling services should be provided to help women prepare for menopause. It shows that 51 respondents (51.0%) strongly agree, 44 respondents (44.0%) agree, 1 respondent (1.0%) is uncertain, and 4 respondents (4.0%) disagree. A strong majority (95.0%) agree that counseling services should be offered, highlighting broad support for such services to help women manage menopause.

Table 17. Whether awareness campaigns about Menopause should be intensified in Gombe Metropolis

Optional Responses	Frequency	Percentage
Strongly Agree	43	43.0%
Agree	50	50.0%
Uncertain	4	4.0%
Disagree	3	3.0%
Total	100	100.0%

Table 17 above depicts respondents' views on whether awareness campaigns about menopause should be intensified in Gombe metropolis. It reveals that 43 respondents (43.0%) strongly agree, 50 respondents (50.0%) agree, 4 respondents (4.0%) are uncertain, and 3 respondents (3.0%) disagree. The majority (93.0%) supports the idea of intensified awareness campaigns, indicating strong backing for greater public education on menopause.

Table 18. Whether Access to Healthcare Services Should Be Improved to Address Menopause-Related Conditions

Optional Responses	Frequency	Percentage
Strongly Agree	47	47.0%
Agree	38	38.0%
Uncertain	15	15.0%
Total	100	100.0%

Table 18 above illustrates respondents' views on whether access to healthcare services should be improved to address menopause-related conditions, where it reveals that Strongly Agree recorded a frequency of 47 (47.0%), Agree recorded 38 (38.0%), and Uncertain recorded 15 (15.0%). The majority of respondents agree that healthcare services should be improved for menopause-related conditions, with a cumulative frequency and percentage of 85 (85.0%).

Table 19. Whether Traditional Remedies Can Be Effective in Managing Pre-Menopausal Symptoms

Optional Responses	Frequency	Percentage
Strongly Agree	27	27.0%
Agree	39	39.0%
Uncertain	31	31.0%
Disagree	2	2.0%
Strongly Disagree	1	1.0%
Total	100	100.0%

Table 19 above illustrates respondents' views on whether traditional remedies can be effective in managing pre-menopausal symptoms, where it reveals that Strongly Agree recorded a frequency of 27 (27.0%), Agree recorded 39 (39.0%), and Uncertain recorded 31 (31.0%). A significant portion of respondents (66.0%) believe that traditional remedies are effective in managing symptoms, although the 31.0% uncertainty highlights a need for further exploration in this area.

Table 20. Whether Employers Should Introduce Policies to Support Menopausal Women in the Workplace

Optional Responses	Frequency	Percentage
Strongly Agree	31	31.0%
Agree	33	33.0%
Uncertain	28	28.0%
Disagree	8	8.0%
Total	100	100.0%

Table 20 shows respondents' views on whether employers should introduce policies to support menopausal women in the workplace, where it reveals that Strongly Agree recorded a frequency of 31 (31.0%), Agree recorded 33 (33.0%), and Uncertain recorded 28 (28.0%). A majority of respondents (64.0%) support the introduction of policies to help menopausal women, although the 28.0% uncertainty suggests differing views among the respondents.

Table 21. Regular Exercise and Balanced Diet

Optional Responses	Frequency	Percentage
Strongly Agree	49	49.0%
Agree	41	41.0%
Uncertain	8	8.0%
Disagree	2	2.0%
Total	100	100.0%

Table 21 indicates the respondents' need to encouraged women to do adopt healthy regular exercise and eat balanced diet, where it reveals that Strongly Agree recorded a frequency of 49 (49.0%), Agree recorded 41 (41.0%), and Uncertain recorded 8 (8.0%). A significant majority (90.0%) agree that healthy lifestyle practices should be encouraged, underlining the importance of these habits for women's well-being.

Table 22. Whether More Research Should Be Conducted to Understand Menopause in the Context of Gombe Metropolis

Optional Responses	Frequency	Percentage
Strongly Agree	51	51.0%
Agree	45	45.0%
Uncertain	3	3.0%
Strongly Disagree	1	1.0%
Total	100	100.0%

Table 22 illustrates respondents' views on whether more research should be conducted to understand menopause in the context of Gombe metropolis, where it reveals that Strongly Agree recorded a frequency of 51 (51.0%), Agree recorded 45 (45.0%), and Uncertain recorded 3 (3.0%). A clear majority (96.0%) of respondents support further research, indicating a strong desire to better understand menopause in the local context.

4. DISCUSSION OF MAJOR FINDINGS

The findings of the study on the primary causes of menopause reveals that hormonal changes were overwhelmingly identified as the most significant factor influencing menopause onset, with 98% of respondents affirming this view.

This consensus supports the widely accepted scientific understanding that menopause is primarily driven by a decline in estrogen and progesterone production as women age (Santoro, 2020). Similarly, the role of genetics in menopause timing was widely acknowledged, with 94% of respondents agreeing or strongly agreeing that family history influences menopause onset. Previous studies have confirmed that women whose mothers experienced early menopause are more likely to follow a similar pattern due to genetic predispositions (Tao et al., 2021). However, while hormonal and genetic factors were strongly agreed upon, there was considerable uncertainty regarding the role of lifestyle factors such as diet and exercise. The findings showed that nearly half of the respondents were uncertain about lifestyle influences, which contrasts with studies suggesting that poor dietary habits and sedentary lifestyles can contribute to early menopause (Zhu et al., 2019).

Additionally, chronic illnesses such as diabetes and hypertension were identified as contributing factors to early menopause, with 76% of respondents supporting this assertion. This aligns with previous research indicating that metabolic disorders can disrupt hormonal balance and accelerate ovarian aging (Kazemi et al., 2022). However, socioeconomic factors were not widely perceived as influential, as 57% of respondents disagreed or strongly disagreed with their role in menopause onset. This contradicts some studies that link low-income status and poor access to healthcare with earlier menopause due to increased exposure to stress and inadequate nutrition (Gold, 2021).

Similarly, environmental toxins did not receive strong support as a cause of premature menopause, with only 32% of respondents agreeing or strongly agreeing. The lack of consensus on this issue suggests that more awareness is needed about how pollutants and chemical exposures affect reproductive health, as studies have found associations between endocrine-disrupting chemicals and ovarian dysfunction (Rodriguez et al., 2020).

Furthermore the study identified stress as a significant factor in menopause timing, with 87% of respondents agreeing or strongly agreeing that high stress levels accelerate menopause. This finding is consistent with research showing that chronic stress leads to elevated cortisol levels, which can impair ovarian function and lead to an earlier onset of menopause (Li et al., 2021).

Overall, the study's findings confirm the widely recognized biological and genetic causes of menopause while revealing mixed perceptions about lifestyle, socioeconomic, and environmental influences. The variations in responses suggest a need for more public health education on the broader determinants of menopause.

The study findings confirm that menopause significantly affects women's mental health, with 90% of respondents acknowledging its role in causing anxiety and depression. This aligns with previous studies that link declining estrogen levels during menopause to increased susceptibility to mood disorders and cognitive decline (Thurston & Joffe, 2021). Similarly, the overwhelming agreement (92%) regarding the effect of signs which include hot flashes and fatigue, underscores the disruptive nature of menopause on daily life. These results correspond with research indicating that vasomotor symptoms are among the most distressing experiences of menopausal transition, often impairing women's overall quality of life (Freeman, 2020). However, when assessing menopause's impact on workplace productivity, the responses were more divided. While 44% believed menopause reduces productivity, a considerable proportion (27%) remained uncertain, and 30% disagreed. This variation may be due to individual differences in symptom severity and workplace accommodations, as some women manage menopause effectively without significant disruptions (Hardy et al., 2019).

Regarding the impact of menopause on relationships with family and friends, 39% of respondents expressed uncertainty, and 28% disagreed or strongly disagreed that menopause significantly affects relationships. This suggests that while emotional and physical symptoms can strain relationships, other personal and social factors may play a more decisive role (Avis et al., 2021). In contrast, awareness of menopause-related health risks, such as osteoporosis and cardiovascular disease, was high, with 87% of respondents agreeing that menopause increases these risks. This is consistent with evidence that declining estrogen levels contribute to bone density loss and heightened cardiovascular vulnerability (Szmuilowicz et al., 2021). Lastly, the effects of sleep disturbances on overall well-being received mixed responses. While 52% agreed that menopause-related sleep disturbances impact well-being, a substantial 39% remained uncertain.

This division may stem from individual variations in sleep patterns and the degree to which sleep disturbances are perceived as problematic (Kravitz et al., 2020).

Overall, these findings reinforce existing knowledge on menopause's effects on mental health, physical symptoms, and long-term health risks. However, variations in perceptions of its impact on productivity, relationships, and sleep disturbances suggest that experiences of menopause are highly individualized. Future research and health interventions should consider these diverse experiences to better support women navigating this transition.

Recommendations

Based on the findings, the following recommendations were proposed:

- Government agencies, healthcare providers, and NGOs should collaborate to implement extensive menopause awareness programs to educate women on its causes, effects, and management strategies.
- Healthcare facilities should be equipped to provide specialized menopause care, including counseling, routine screenings for osteoporosis and cardiovascular risks, and access to hormonal and non-hormonal treatment options.
- Employers should introduce policies that provide flexible working arrangements, wellness programs, and mental health support for menopausal employees to mitigate workplace productivity losses.
- Government and private health insurance schemes should incorporate coverage for menopause-related healthcare needs to alleviate financial burdens on affected women.
- Public health initiatives should emphasize the benefits of balanced diets, regular exercise, and stress management techniques to mitigate menopause-related health risks.
- Academic institutions and research bodies should conduct more studies to explore effective traditional remedies and alternative treatments for managing menopause symptoms in Nigerian contexts.

CONCLUSION

This study confirms that menopause is primarily influenced by biological and genetic factors, though lifestyle, stress, and chronic illnesses also play contributory roles. The effects of menopause are diverse, impacting mental health, physical well-being, and, to some extent, workplace productivity and relationships. The findings highlight that while awareness of menopause-related health risks is high, misconceptions and uncertainty remain regarding lifestyle influences and traditional remedies. The study underscores the need for enhanced public health education, workplace accommodations, and access to quality healthcare services to support menopausal women in Gombe Metropolis. Addressing these issues through structured policies, awareness campaigns, and healthcare improvements can significantly enhance the well-being and quality of life for menopausal women.

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CHAPTER 3
HUMAN MYIASIS: A MULTIDISCIPLINARY PERSPECTIVE ON DIPTERAN INFESTATIONS

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INTRODUCTION

Myiasis is a parasitic condition characterized by the infestation of tissues and organs of humans and other vertebrates by dipteran larvae, which feed, at least during part of their biological cycle, on living or necrotic tissue, organic secretions, or food material ingested by the host (Avula et al., 2011; Francesconi & Lupi, 2012).

From a conceptual standpoint, it is a condition that can be understood from different perspectives within the fields of parasitology and dermatology. In this context, myiasis is frequently classified as a dermatozoonosis, defined by the infestation of vertebrate animal tissues (mammals, birds, reptiles, and amphibians) by fly larvae, which may deposit their eggs in natural orifices, in skin continuity breaches, or, in some cases, in intact skin, as observed in the furuncular form (Rodrigues et al., 2021). The condition can also be understood as a cutaneous infestation caused by dipteran larvae, being frequently described as a zoodermatose, since it results directly from the action of animal organisms on human tissues (Barnabé et al., 2016).

Additionally, it is considered a form of ectoparasitosis, since the larvae develop on the surface or in accessible cavities of the host, establishing a transitory yet potentially destructive parasitic relationship (Barros, 2017; Cuestas et al., 2021). Regardless of the terminology adopted, there is a consensus in the literature that myiasis results from the invasion of living or dead tissues by larvae belonging to the order Diptera, whose feeding activity is intrinsically associated with tissue degradation (Barnabé et al., 2016; Francesconi & Lupi, 2012).

The classic definition proposed by Zumpt, in 1965, remains widely accepted, establishing that myiasis occurs when fly larvae feed on the host's tissues, their bodily secretions, or ingested material, during at least one stage of their development (Fares et al., 2005; Hall et al., 2016).

Although it may present a benign course, it can have not only destructive consequences for human tissue, but also cause additional infections or psychosocial problems; that is, the invasion can become dangerous, resulting in severe tissue disturbances, secondary infections, and, in extreme cases, the patient's death (Avula et al., 2011; Bernhardt et al., 2018).

Myiasis is also a dermatological complication that reaches a level of critical severity when associated with oncological processes (Donato-Rondón et al., 2025; Francesconi & Lupi, 2012).

Notwithstanding its historical recognition as a veterinary pest of immense economic impact on cattle and sheep herds, human myiasis is considered a neglected disease, intimately linked to poverty and the precariousness of sanitary infrastructure (Barnabé et al., 2016; Donato-Rondón et al., 2025). The clinical impact is vast, ranging from self-limiting cutaneous infestations to devastating cavitary conditions with destruction of noble tissues, severe hemorrhages, and invasion of the central nervous system, potentially culminating in the host's death (Cencil et al., 2006; Fares et al., 2005).

The recognition of flies as causative agents of myiasis dates back to antiquity, being considered some of the most devastating insects in the world (Francesconi & Lupi, 2012). The etymology of the term "myiasis" derives from the Greek roots "myia," which means fly, and "iasis," which means disease (Cavalcanti, 2008; Francesconi & Lupi, 2012; McGraw & Turiansky, 2008; Rana et al., 2020). The nomenclature was formally proposed or coined by Reverend Frederick William Hope in 1840 (Hope, 1840; Khandelwal et al., 2025), although it was presented for the first time by Laurence in 1909 (Gomes-Ferreira et al., 2014; Khandelwal et al., 2025). Hope aimed to create an umbrella term to group human pathologies caused specifically by dipteran larvae, distinguishing them from other conditions caused by insects (Gomes-Ferreira et al., 2014; Hope, 1840).

In the specific field of stomatology, the first detailed description of a larval infestation affecting the human oral cavity was performed by Laurence in 1909 (Cavalcanti, 2008; Laurence, 1909). Since then, the literature has evolved from anecdotal reports to complex biological analyses, including the molecular biology and genomics of the species involved (Tandonnet et al., 2022). Risk factors for myiasis include low socioeconomic status, poor hygiene, poverty, and advanced age (Francesconi & Lupi, 2012; Lwanga et al., 2018; Marquez et al., 2007). Susceptibility is aggravated by comorbidities such as psychiatric diseases, alcoholism, weakness, diabetes mellitus, and occlusive vascular disease (Ali et al., 2025; Azarmi et al., 2024; Lwanga et al., 2018; Yadav et al., 2023).

Additionally, the physical incapacity for self-protection against flies, common in bedridden patients or those with neurological deficits, is a determinant factor for the deposition of eggs and larvae (Albarrak et al., 2025; Avula et al., 2011).

Despite knowledge of these factors, there is a scarcity of precise epidemiological data, which makes the true global impact of human myiasis unknown (Azarmi et al., 2024; Cuestas et al., 2021; Lwanga et al., 2018). The lack of a central compulsory notification system in most endemic countries and the variation in the quality of medical records hinder the acquisition of reliable statistics on the prevalence of the disease (Donato-Rondón et al., 2025; Francesconi & Lupi, 2012).

The lack of data on human myiasis is partially explained by the fact that many healthcare professionals consider it a disease of minor importance and, therefore, do not report the cases (Lwanga et al., 2018). Consequently, cases are not reported to public health authorities, and larvae and dressings are frequently discarded without careful examination or laboratory identification (Cuestas et al., 2021; Francesconi & Lupi, 2012; Lwanga et al., 2018).

Additionally, the social stigma and demoralizing perception of the disease lead many patients and their families to seek domestic empirical treatments (Chang et al., 2025; Cuestas et al., 2021; Francesconi & Lupi, 2012; Lwanga et al., 2018). Such behavior reduces the number of cases attended and properly documented in medical services, leading to the cycle of less invisibility of this condition as a tropical disease, often neglected (Barnabé et al., 2016; Marquez et al., 2007; Monney et al., 2025).

1. TAXONOMY AND FAMILIES OF DIPTERA OF MEDICAL IMPORTANCE

Flies that infest humans belong primarily to the order Diptera, characterized by true flies, that is, those whose adults possess two wings (McGraw & Turiansky, 2008). The order Diptera houses more than 150 species documented as etiological agents of human myiasis (Cavalcanti, 2008; Cencil et al., 2006). However, globally, approximately 37 species of flies, belonging to ten families, are responsible for myiasis in humans (Singh & Singh, 2015).

Nevertheless, the vast majority of clinical cases are attributed to three main families of the group Calyptratae: Calliphoridae (blow flies), Sarcophagidae (flesh flies), and Oestridae (bot flies) (Avula et al., 2011; Singh & Singh, 2015).

Calliphoridae: The species Cochliomyia hominivorax (new world screwworm fly) stands out, described by Coquerel in 1858 as an extremely aggressive species that invades human frontal sinuses (Barnabé et al., 2016; Tandonnet et al., 2022). The adult measures about 8 mm, with a metallic-green body and bluish reflections (Cencil et al., 2006). Another critical species is Chrysomya bezziana (of the Old World), prevalent in Asia and Africa (McGraw & Turiansky, 2008; Singh & Singh, 2015). Recent genomic research has presented the first chromosome-scale genome assembly of C. hominivorax, facilitating studies on parasitism and insecticide resistance (Tandonnet et al., 2022).

Oestridae: The emblematic species in the Americas is Dermatobia hominis (human botfly), which occurs from Mexico to Argentina (Barnabé et al., 2016; Fares et al., 2005). Other species such as Hypoderma bovis and Gasterophilus intestinalis are known to cause migratory myiasis (McGraw & Turiansky, 2008; Sun, 2025).

Sarcophagidae: Known as flesh flies, with emphasis on the genus Sarcophaga and the species Wohlfahrtia magnifica (Azarmi et al., 2024; Robins & Khachemoune, 2010). It includes the genus Wohlfahrtia, with W. magnifica being an obligatory parasite in the Mediterranean and Eurasia (McGraw & Turiansky, 2008; Singh & Singh, 2015). Species from families such as Muscidae (Musca domestica), Fanniidae, Phoridae, and Syrphidae (Eristalis tenax) are common agents of facultative or accidental myiasis (Singh & Singh, 2015).

2. PARASITOLOGICAL CLASSIFICATION AND BIOLOGICAL BEHAVIOR

The classification of myiasis is based on the biological necessity of the larva in relation to the host to complete its life cycle (Barnabé et al., 2016; Francesconi & Lupi, 2012).

2.1 Obligatory or Primary Myiases (Biontophagous)

In this category, larvae develop exclusively in the tissues of living vertebrates, this being an indispensable stage to complete their life cycle (Barnabé et al., 2016; Cavalcanti, 2008; Cencil et al., 2006).

They are highly specialized species that possess sophisticated mechanisms to evade the host's immune system and can cause massive and rapid tissue destruction (Bernhardt et al., 2018; Marquez et al., 2007). C. hominivorax is attracted to fresh wounds or natural orifices, depositing masses of 20 to 400 eggs; the larvae hatch in less than 24 hours and feed voraciously on healthy tissue (Barnabé et al., 2016; Cencil et al., 2006). D. hominis utilizes phoresis: the female captures a hematophagous insect and deposits her eggs on its abdomen (Barnabé et al., 2016; Fares et al., 2005). When the vector bites the host, body heat stimulates the hatching of the larvae, which penetrate the skin (Barnabé et al., 2016).

2.2 Facultative Or Secondary Myiases (Necrobiontophagous)

Facultative larvae normally develop in decomposing organic matter (carcasses or refuse), but they can opportunistically infest necrotic tissues, infected wounds, or areas with accumulated secretions in living hosts (Francesconi & Lupi, 2012; Yıldırım et al., 2025). They are attracted by the foul odors of chronic ulcers or infected wounds (Shimada et al., 2025). Examples include the genera Lucilia, Sarcophaga, and Musca (Cavalcanti, 2008; Shimada et al., 2025).

2.3 Pseudomyiases and Accidental Infestations

They result from the accidental ingestion of eggs or larvae present in contaminated food or water, passing through the gastrointestinal tract without establishing a true parasitic cycle, although they may cause digestive disorders (Barnabé et al., 2016; Cavalcanti, 2008). Although it is not the natural habitat for larval development, the larvae can survive temporarily in the gastrointestinal tract, causing nausea, vomiting, and diarrhea (Cencil et al., 2006; Francesconi & Lupi, 2012).

3. GLOBAL EPIDEMOLOGY AND THE IMPACT OF CLIMATE CHANGE

Myiasis is endemic in tropical and subtropical regions due to the warm and humid climate that favors the life cycle of dipterans (Azarmi et al., 2024; Barnabé et al., 2016). In South American countries such as Colombia, the spatial distribution of bioagents is strongly influenced by altitude, with the observation that species richness decreases at high altitudes (Donato-Rondón et al., 2025). Lowland temperatures and humidity promote greater decomposition of organic matter, which favors biodiversity and fly population density (Donato-Rondón et al., 2025). Species such as the human botfly (Dermatobia hominis) present clear adaptive limits, being rare above 1,400 meters and extremely frequent in the 600-meter altitude range, where they seek humid microclimates and dense vegetation (Borja, 2003).

The travel medicine phenomenon has brought myiasis to previously unaffected regions, such as Europe, where tourists return from tropical areas with infestations by D. hominis or Cordylobia anthropophaga (Bernhardt et al., 2018; Francesconi & Lupi, 2012). Thus, in developed countries, most cases are diagnosed in travelers returning from endemic areas, being considered the fourth most common travel-associated skin disease (Bernhardt et al., 2018; Francesconi & Lupi, 2012).

In temperate climate zones, the occurrence of the disease presents strict seasonality, being practically restricted to the spring and summer months due to the thermal dependence of the larvae (Cavalcanti, 2008; Lwanga et al., 2018). The warm environment acts as a biological catalyst that accelerates the development stages from egg to larva and pupa, shortening the life cycle and allowing the rapid proliferation of flies (Monney et al., 2025; Rana et al., 2020).

However, global warming and climate change are altering this dynamic. The increase in average temperatures allows tropical flies to invade new regions in Europe and North America, raising the risk of autochthonous cases in previously temperate areas (Bernhardt et al., 2018; Hall et al., 2016).

Under this new climatic perspective, myiasis transcends the status of a neglected pathology of rural areas to become a critical hospital hygiene problem in high-income countries (Monney et al., 2025).

Persistent heatwaves facilitate the introduction of new pathogen vectors into urban environments and intensive care units (ICUs), where vulnerable and sedated patients become preferred targets for egg-laying (Monney et al., 2025). Additionally, global animal transport and tourism facilitate the inadvertent dispersal of pathogens (Hall et al., 2016).

The population dynamics of these dipterans in response to climate suggest that control and eradication strategies must necessarily be linked to seasonal variations (Souza et al., 2025). During cold or dry periods, fly populations suffer drastic reductions and concentrate in "climatic refuges" (Souza et al., 2025). Identifying and managing these refuges is crucial to prevent these areas from acting as sources of recolonization when climatic conditions become favorable again, which could compromise the efficacy of integrated management programs (Souza et al., 2025).

Global climate changes are altering the epidemiological scenario. The increase in average temperatures allows tropical species to colonize higher latitudes (Bernhardt et al., 2018). Autochthonous cases of myiasis caused by C. anthropophaga have been described in Portugal, suggesting the expansion of this species from the African to the European continent (Bernhardt et al., 2018).

4. PREDISPOSING RISK FACTORS AND SOCIOECONOIC ASPECTS

Far beyond an isolated pathology, myiasis is frequently recognized as a direct reflection of certain types of neglect. The literature indicates that the infestation is almost invariably intertwined with scenarios of socioeconomic fragility and certain privations of fundamental or basic rights, as well as linked to biological and cognitive fragility (in cases of Alzheimer's disease or other dementias, the impairment of self-care and functional dependence become determinant factors that facilitate the onset of the infestation, evidencing that vulnerability, at times, stems from the individual's own incapacity for self-protection).

In this context, myiasis is frequently described as a disease associated with social vulnerability, with its occurrence being closely related to conditions of social vulnerability and exclusion (Freitas et al., 2012; Marquez et al., 2007).

Debilitated elderly people, small children, and individuals with neurological or psychiatric disorders (e.g., Alzheimer's, Parkinson's, cerebral palsy) are identified as risk groups, as they are the most affected by the incapacity for self-care and the inability to ward off flies (Fares et al., 2005; Marquez et al., 2007; Rodrigues et al., 2021).

The main predisposing factors include:

Hygiene and Sanitation: The lack of piped water, the accumulation of garbage near residences, and the presence of open sewers create massive breeding sites for fly proliferation (Barnabé et al., 2016; Rodrigues et al., 2021). In Rio de Janeiro, Brazil, a study showed that 62% of patients with myiasis lived on less than three minimum wages established in the country (Marquez et al., 2007).

Comorbidities: A detailed analysis of the sources reveals that systemic comorbidities play a central role in patients' vulnerability to myiasis, acting as facilitators of infestation through the degradation of tissue integrity and the impairment of the immune response.

Systemic comorbidities, such as diabetes mellitus, are identified as one of the main intrinsic risk factors, appearing with high prevalence in several case series (Cuestas et al., 2021; Rana et al., 2020). Diabetes predisposes to myiasis due to failures in the microvasculature and in connective tissue repair processes, which often results in the development of difficult-to-heal lesions, such as diabetic foot ulcers, which serve as a niche for larval deposition (Bernhardt et al., 2018; Cuestas et al., 2021; Rodrigues et al., 2021). Similarly, peripheral vascular diseases (or occlusive vascular diseases) are frequently associated with gangrene and chronic ulcers, significantly increasing the attractiveness for dipterans (Azarmi et al., 2024; Lwanga et al., 2018; McGraw & Turiansky, 2008).

Senility, or advanced age, is another determining factor, as it is often accompanied by a general decrease in physical resistance and the coexistence of multiple chronic pathologies that limit the individual's ability to perform self-care (Albarrak et al., 2025; Azarmi et al., 2024; McGraw & Turiansky, 2008). In many cases, the state of generalized debility in the elderly is what allows flies to deposit their eggs undisturbed (Albarrak et al., 2025; Pessoa & Galvão, 2011).

Chronic alcoholism and substance use are widely documented as factors that increase risk, not only by systemically debilitating the host, but by reducing the level of consciousness and vigilance against insects (Cavalcanti, 2008; Freitas, 2012; Rana et al., 2020; Yadav et al., 2023). Malnutrition considerably worsens this scenario, since malnourished individuals present a reduced cellular regenerative capacity and a weakened immune system, making infestations more aggressive and rapidly evolving (Cavalcanti, 2008; Freitas, 2012; Marquez et al., 2007).

Other conditions of immunosuppression or chronic infectious diseases, including HIV, tuberculosis, and leprosy, are also reported in the literature as systemic states that increase susceptibility to larval colonization (Cuestas et al., 2021; Francesconi & Lupi, 2012; Rana et al., 2020).

Neurological and Psychiatric Conditions: Patients with neuropsychomotor deficits, cerebral palsy, Alzheimer's disease, or psychiatric disorders present a higher risk due to their inability to self-protect and perform hygiene (Gomes-Ferreira et al., 2014; Sadaksharam & Muralidharan, 2025).

Exposed Wounds: Exposed wounds, whether of traumatic origin, vascular ulcers, surgical, or malignant lesions, become primary focal points of attraction for gravid female dipterans, especially when they present signs of secondary infection and tissue necrosis (Azarmi et al., 2024; Marquez et al., 2007). The fundamental mechanism in this process resides in the release of a foul odor originating from the emission of volatile organic compounds derived from tissue decomposition and suppuration, which act as potent chemical attractants for gravid females (Cuestas et al., 2021). In cases of malignant wounds, such as squamous and basal cell carcinomas, the chronicity of the lesion and the presence of devitalized tissue provide an ideal substrate for voracious larval development, which can result in deep tissue destruction and invasion of adjacent structures (Azarmi et al., 2024; Cuestas et al., 2021). In the hospital context, the maintenance of invasive devices, such as tracheostomy cannulas and orotracheal tubes in immobilized patients, creates moist microenvironments rich in secretions that facilitate larval deposition, especially when there are failures in physical protective barriers (Albarrak et al., 2025; Rana et al., 2020).

Anatomical Factors (Oral Myiasis): The occurrence of myiasis in the oral cavity is a rare pathological manifestation, frequently associated with a disruption in biological homeostasis and the prolonged exposure of intraoral tissues to the external environment (Ali et al., 2025; Avula et al., 2011; Cavalcanti, 2008). In healthy individuals, adequate lip seal and the defensive properties of salivary flow function as robust physiological barriers against the invasion of dipteran larvae; however, structural alterations and chronic inflammatory processes may establish favorable ecological niches for the oviposition of gravid females (Avula et al., 2011; Cavalcanti, 2008; Yıldırım et al., 2025). Consequently, scientific literature identifies specific predisposing conditions that facilitate larval access to deep tissues and compromise local hygiene (Francesconi & Lupi, 2012; Gomes-Ferreira et al., 2014). Within the scope of localized morphological and pathological variations, the following anatomic factors are prominent: mouth breathing, labial incompetence, anterior open bite, and advanced periodontal disease (Avula et al., 2011; Cavalcanti, 2008).

5. CLINICAL AND ANATOMICAL CLASSIFICATION OF INFESTATIONS

The clinical presentation of myiasis is classified according to the depth of invasion and the anatomical site affected (Barnabé et al., 2016; Francesconi & Lupi, 2012).

5.1 Cutaneous Myiasis: Furuncular, Migratory, And Wound (Traumatic)

Furuncular: It is characterized by an erythematous nodule similar to a boil (furuncle), with a punctiform central orifice for larval respiration (Cuestas et al., 2021; McGraw & Turiansky, 2008). The patient frequently reports the sensation of "stinging" or movement under the skin, especially at night (Cuestas et al., 2021). It is primarily caused by Dermatobia hominis and Cordylobia anthropophaga (McGraw & Turiansky, 2008; Robins & Khachemoune, 2010).

Migratory (Creeping Myiasis): Larvae such as Gasterophilus or Hypoderma penetrate the dermis and create pruritic serpiginous tunnels, resembling cutaneous larva migrans (Cuestas et al., 2021; Francesconi & Lupi, 2012).

Wound (Traumatic): This occurs in pre-existing open lesions (colonization of chronic ulcers or exposed wounds). It is the most common form of Cochliomyia hominivorax, where hundreds of larvae can invade deep tissues destructively, potentially leading to extensive areas of tissue destruction (Cuestas et al., 2021; McGraw & Turiansky, 2008; Singh & Singh, 2015).

5.2 Cavitary Myiasis of the Head and Neck (Oral, Nasal, Ocular, And Aural)

Oral: Associated with severe halitosis, poor oral hygiene, and mouth breathing (Cavalcanti, 2008; Gomes-Ferreira et al., 2014). It frequently affects the palate and anterior gingiva (Cavalcanti, 2008). The occurrence of myiasis in the oral cavity is uncommon, since oral tissue is rarely exposed to the external environment (Khandelwal et al., 2025).

Oral myiasis is commonly attributed to predisposing anatomical and medical conditions, such as prolonged exposure of the oral cavity to the external environment, mouth breathing, anterior open bite, and incompetent lips (Khandelwal et al., 2025). In this sense, other conditions that can cause myiasis include cerebral palsy, tooth extraction, neglected mandibular fracture in patients undergoing mechanical ventilation, and certain local pathological conditions, such as cancrum oris and malignancies (Khandelwal et al., 2025).

Nasal: Nasal myiasis is characterized as the infestation of the nasal cavity by dipteran larvae, whose flies deposit their eggs directly inside the nasal cavity or in its vicinity (Francesconi & Lupi, 2012; Singh & Singh, 2015). This pathology presents clinically with episodes of nasal obstruction, foul-smelling rhinorrhea, and facial pain (Francesconi & Lupi, 2012; Rana et al., 2020). In severe cases, the larvae can perforate the septum and invade the ethmoid sinus or the orbit (Rana et al., 2020). Cases occur more frequently in people who suffer from atrophic rhinitis, a condition that reduces the sneezing reflex and dilates the nasal cavity, facilitating the entry and attachment of the parasites (Francesconi & Lupi, 2012; Marquez et al., 2007).

The signs and symptoms of nasal myiasis are generally related to the presence and movement of the larvae, including a foreign-body sensation, with or without a sensation of movement; nasal pain; facial pain; blood-stained or mucopurulent nasal discharge; epistaxis; foul odor; and anosmia (Francesconi & Lupi, 2012; Rana et al., 2020).

Aural (Otomyiasis): It involves the external and middle ear canal and can cause tympanic perforation, intense otalgia, and deafness (Rana et al., 2020; Tbini et al., 2022). Pre-existing clinical conditions, such as chronic suppurative otitis media, are identified as determining risk factors, as purulent discharge and foul odor act as potent attractants for the oviposition of female flies (Rana et al., 2020; Singh & Singh, 2015; Tbini et al., 2025).

Symptoms of auricular myiasis may include itching, bleeding, tinnitus, and restlessness; crawling sensations and buzzing noises may also occur (Singh & Singh, 2015). Severe infestations can lead to foul-smelling ear discharge (Singh & Singh, 2015). In addition to severe pain and tinnitus, larval activity can destroy the hearing ossicles and cause bone erosion with a risk of intracranial invasion (Francesconi & Lupi, 2012; Tbini et al., 2022).

Ocular (Ophthalmomyiasis): It can be external (in the eyelids or conjunctiva) or internal (invasion of the anterior or vitreous chamber), the latter being an emergency with the risk of total loss of vision (Francesconi & Lupi, 2012; Rodriguez et al., 2003).

Additionally, ophthalmomyiasis can evolve into critical states of anatomical destruction, particularly when associated with predisposing factors such as eyelid carcinomas or poor hygiene conditions that favor infestation (Barnabé et al., 2016; Cuestas et al., 2021; Francesconi & Lupi, 2012).

As discussed by Francesconi and Lupi (2012), the external form is usually initially self-limited, manifesting with a foreign body sensation, conjunctival hyperemia, and acute tearing; however, larval migration can reach the lacrimal glands and even the nasal cavity through the lacrimal canal.

Clinical severity increases exponentially in internal ophthalmomyiasis and orbital myiasis; in these scenarios, deep invasion by larvae can cause severe panuveitis, exudative retinal detachment, and the appearance of atrophic pigmentary tracks in the retinal epithelium, frequently culminating in irreversible functional loss of the organ and blindness (Francesconi & Lupi, 2012; Singh & Singh, 2015). Investigations by Cuestas et al. (2021) and Rodriguez et al. (2003) emphasize that in elderly patients with neglected malignant orbital tumors, massive infestation can lead to total necrosis of intraorbital structures and bone invasion, requiring precise diagnoses via computed tomography and urgent interventions to mitigate pain, eliminate the larvae, and enable subsequent curative or palliative surgical approaches.

5.3 Myiasis of Internal Organs (Urogenital And Gastrointestinal)

Urogenital myiasis occurs in conditions of extremely poor hygiene, uterine prolapses, or the use of underwear dried outdoors where flies deposit eggs (Azad et al., 2025; Singh & Singh, 2015). A case was reported in a 5-year-old boy in Iran (Azad et al., 2025).

The gastrointestinal form occurs through the accidental ingestion of eggs/larvae and manifests with nausea, vomiting, and diarrhea (Francesconi & Lupi, 2012).

5.4 Myiasis in Special Settings: Nosocomial and Associated with Malignancies

Nosocomial: Infestations acquired in hospitals or intensive care units (ICUs), generally in patients who are sedated, intubated, or have compromised consciousness (Khandelwal et al., 2025; Monney et al., 2025).

Malignancies: Ulcerated cancers, such as Squamous Cell Carcinoma (SCC) and Basal Cell Carcinoma (BCC), are classic focal points. The necrotic odor attracts necrobiontophagous flies (Cuestas et al., 2021; Pessoa & Galvão, 2011; Rodriguez et al., 2003).

6. PATHOGENESIS AND COMPLICATIONS: TISSUE DESTRUCTION, SEPSIS, AND SEQUELAE

The larvae exert their pathogenic action through the secretion of proteolytic enzymes and collagenases that digest the tissues, facilitating invasion (Cencil et al., 2006; Rana et al., 2020). The rotational movement of the larvae, aided by oral hooks and body spines, causes laceration of small vessels, leading to hemorrhages and edema (Rana et al., 2020).

Therefore, the larvae cause damage through the mechanical action of their mouth hooks and body spines, and by the release of digestive proteolytic enzymes (Cencil et al., 2006; Singh & Singh, 2015).

The complications can be devastating and include:

Secondary Infections: The presence of larvae and their metabolic waste predisposes to serious bacterial infections (Singh & Singh, 2015).

Tissue invasion by these organisms can result in severe systemic complications, potentially even leading to death due to toxemia or septicemia when the larvae invade body cavities or areas that prevent their direct visualization (Singh & Singh, 2015). Exposure to digestive enzymes and toxins secreted by wild fly larvae significantly increases the risk of bacterial infection and destruction of host tissues (Cuestas et al., 2021). Exposure to digestive enzymes and toxins secreted by wild fly larvae significantly increases the risk of bacterial infection and destruction of host tissues (Cuestas et al., 2021). These toxic substances are responsible for triggering intense inflammatory processes that sabotage the natural healing of the wound (Rana et al., 2020; Sadaksharam & Muralidharan, 2025). In addition to the physical presence, "larval residues" and liquid excretions function as persistent focal points of infection if they are not properly removed (Marquez et al., 2007). Also, the accidental laceration of larvae during extraction procedures releases fragments that provoke extremely serious foreign body inflammatory reactions (Boggild et al., 2002). The literature highlights that fly contact with exposed wounds can lead to infections with antimicrobial-resistant bacteria, and flies are, at least, responsible for the transmission of Chlamydia trachomatis, which causes trachoma (Bernhardt et al., 2018). Clinicians should focus on the treatment of secondary bacterial infections and the proper debridement of maggot-infested wounds (Singh & Singh, 2015).

Meticulous debridement of necrotic tissue is an essential step to enable correct tissue repair and eliminate substrates that attract new vectors (Gomes-Ferreira et al., 2014). Thus, the standard treatment protocol involves a combination of exhaustive mechanical removal of the larvae with surgical debridement when necessary (Shimada et al., 2025). The administration of broad-spectrum antibiotic therapy is fundamental for reducing the duration of infection and optimizing the patient's recovery period (Gomes-Ferreira et al., 2014). In pediatric practice, it is observed that approximately 88% of patients received systemic antibiotics specifically to prevent or treat secondary bacterial complications (Rodrigues et al., 2021). Systemic antibiotics (cephalosporins, amoxicillin) are often necessary to treat secondary infections (Gomes-Ferreira et al., 2014; Rodrigues et al., 2021).

Sepsis: The introduction of bacteria by the larvae or the secondary infection of open wounds can lead to septic shock and death (Lysaght et al., 2018; Muñoz et al., 2021).

Osteomyelitis: Deep tissue invasion can lead to bone infection, as demonstrated in cases of cranial osteomyelitis in children (Muñoz et al., 2021).

Bone Destruction: Reported in cases of facial and orbital myiasis (Cuestas et al., 2021; Muñoz et al., 2021).

Destruction of Vital Organs: Cerebral invasion (cerebral myiasis), complete ocular destruction, or airway obstruction are fatal emergencies (Rana et al., 2020; Yadav et al., 2023).

7. DIAGNOSIS: CLINICAL EVALUATION, IMAGING, AND ENTOMOLOGICAL IDENTIFICATION

The diagnosis is predominantly clinical, based on direct visual inspection and the observation of motile larvae in the tissue (Fares et al., 2005; Yıldırım et al., 2025). The characteristic foul odor and purulent discharge are frequent signs (Albarrak et al., 2025).

Imaging exams such as Computed Tomography (CT) aid in evaluating the extent of tissue damage, although they may fail to detect small or superficial larvae (Albarrak et al., 2025; Rodriguez et al., 2003).

Computed Tomography and Magnetic Resonance Imaging (MRI) are also vital for delimiting the depth of invasion and detecting intracranial involvement or bone erosion (Cuestas et al., 2021; Rodriguez et al., 2003). Ultrasonography can be useful for identifying subcutaneous larvae (McGraw & Turiansky, 2008).

Definitive entomological identification requires the morphological analysis of posterior spiracles and oral hooks by specialists (entomologists) or the rearing of larvae to the adult stage for species classification (Cencil et al., 2006; Monney et al., 2025). For the proper fixation and preservation of collected specimens, it is recommended that larvae be preserved in containers containing 70% alcohol (Cavalcanti, 2008; Rodrigues et al., 2017). Aiming for a safe and specific taxonomic diagnosis, it is advised to allow part of the larvae to complete their biological cycle (pupation) to the adult stage, at which point the observation of morphological characters becomes definitive (Cencil et al., 2006; Rodrigues et al., 2017).

8. THERAPEUTIC APPROACHES AND CLINICAL MANAGEMENT

The primary objective is the complete elimination of the larvae and infection control.

8.1 Mechanical Removal and Asphyxiation Techniques

The treatment of choice is careful manual extraction with forceps, ensuring that the larva is not fragmented (Cavalcanti, 2008; Cencil et al., 2006). Manual removal with forceps is the treatment of choice and should be performed with caution to avoid the fragmentation of the larvae, which could trigger intense inflammatory reactions or abscesses (Fares et al., 2005; Gomes-Ferreira et al., 2014).

To facilitate extraction, asphyxiating agents are used that obstruct the larvae's respiratory orifices, forcing their migration to the surface. Cited substances include: turpentine oil, solid Vaseline (petroleum jelly), liquid paraffin, ethyl ether, bacon, and chloroform (Avula et al., 2011; Gomes-Ferreira et al., 2014; McGraw & Turiansky, 2008). Exposure to tolerable sunlight can also stimulate the larvae to leave deep niches (Avula et al., 2011).

8.2 Pharmacotherapy: Systemic and Topical Use of Ivermectin

Ivermectin, a semi-synthetic macrolide, has revolutionized the treatment of cavitary and orbital myiasis. It acts by blocking nerve impulses via gamma-aminobutyric acid (GABA), causing larval paralysis and death (Gomes-Ferreira et al., 2014; Rodriguez et al., 2003). Ivermectin is reported as being very effective in the systemic control of larvae at different stages of development and presents few side effects (Rodriguez et al., 2003). It is reported that a single oral dose proves effective in eliminating larvae in deep tissues where mechanical removal is impossible (Rodrigues et al., 2017; Rodriguez et al., 2003). The topical use of 1% ivermectin solutions is also reported with success (Cencil et al., 2006; Francesconi & Lupi, 2012).

8.3 Surgical Debridement and Control of Secondary Infections

In cases of massive infestations, extensive necrosis, or deep invasion, surgical debridement under general anesthesia may be necessary to remove non-viable tissues and remaining larvae (Albarrak et al., 2025; Gomes-Ferreira et al., 2014). Broad-spectrum antibiotic therapy (such as amoxicillin, cephalexin, or ceftriaxone) is essential to treat or prevent secondary bacterial infections (Avula et al., 2011; Rodrigues et al., 2021).

9. MEDICAL AND FORENSIC APPLICATIONS

9.1 Myiasis in Forensic Entomology and Investigation of Neglect

The presence and developmental stage of larvae can serve as biological markers to estimate the minimum time of neglect in children, the elderly, or people with disabilities under the care of third parties (Barros, 2017). Through the larval developmental stage and temperature, experts can estimate the Post-Mortem Interval (PMI) or the period during which the victim was left without hygiene care (Barros, 2017).

Based on the scientific evidence presented in the documentary corpus, the use of forensic entomology in clinical contexts proves to be a robust instrument for the protection of vulnerable individuals, allowing for the transposition of biological data into expert evidence of neglect (Barros, 2017).

A high-precision clinical and forensic example was documented by Thyssen et al. (2012) and discussed by Barros (2017) as a primary example to demonstrate the application of forensic entomology in cases of neglect. In the study, they analyzed a 95-year-old patient with Alzheimer's and Parkinson's diseases, diagnosed with a severe case of oral myiasis (Barros, 2017; Thyssen et al., 2012). During clinical management, 87 larvae were collected from the patient's oral cavity, which were morphologically identified as belonging to the species Cochliomyia hominivorax (Barros, 2017; Thyssen et al., 2012). Through the analysis of the length and maturation stage of these specimens — and considering that flies are attracted to open wounds or a lack of hygiene to deposit eggs — the researchers applied temperature-calibrated larval development tables to determine the age of the infestation (Barros, 2017). The entomological study estimated that the myiasis had been present for at least 143 hours (approximately six days) (Barros, 2017; Thyssen et al., 2012). This temporal evidence was decisive in legally questioning the diligence and care of the responsible caregivers, as the calculated interval proved that the patient remained for nearly a week without the necessary oral hygiene or surveillance, materially constituting the omission of indispensable care (Barros, 2017; Thyssen et al., 2012).

Thus, myiasis in incapacitated patients ceases to be just a biological pathology and becomes an indicator of neglect, allowing health professionals to assist the justice system in the classification of crimes of maltreatment or violations of the rights of the elderly and disabled.

9.2 Larval Therapy (Biosurgery) in the Treatment of Chronic Wounds

Paradoxically, sterile larvae of Lucilia sericata are used in a controlled manner in larval debridement therapy to treat infected chronic wounds and difficult-to-heal ulcers (Bernhardt et al., 2018; Shimada et al., 2025). They act by removing necrotic tissues and combating multi-resistant bacteria through antimicrobial secretions (Bernhardt et al., 2018; Hall et al., 2016).

The larvae used in debridement therapy are reared under controlled laboratory conditions, with a specific number of particular species, previously sterilized, significantly reducing the risk of bacterial infection and tissue destruction (Cuestas et al., 2021).

This modality, also called biotherapy or biosurgery, is based on the application of live laboratory-reared larvae that secrete proteolytic enzymes to liquefy necrotic tissue, which is then ingested, favoring granulation and the reduction of lesion odor (Cuestas et al., 2021). The biological efficacy of these larvae extends to the destruction of pathogens resistant to modern antibiotics, such as methicillin-resistant Staphylococcus aureus, through potent antimicrobial compounds that modulate the inflammatory response and eliminate bacterial biofilms (Hall et al., 2016). Although it may represent a low-cost and high-efficiency tool for health systems, its adoption still faces challenges such as certain professional prejudice and the need for rigorous taxonomic control to ensure that only species with necrophagous behavior are used in the clinical setting (Cuestas et al., 2021).

10. PREVENTION MEASURES, HEALTH EDUCATION, AND FLY POPULATION CONTROL

Prevention is based on three pillars: primary prevention focuses on reducing exposure (Barnabé et al., 2016) or avoiding contact with flies, early treatment of wounds, and vector population control (Mohammadi et al., 2024). Prevention measures that can be adopted:

Individual Measures: Use of screens on doors and windows, mosquito nets, repellents, appropriate clothing, and rigorous cleaning of any skin lesion (Barros, 2017; McGraw & Turiansky, 2008). Wounds must be rigorously cleaned and covered (Pessoa & Galvão, 2011).

Health Education: Training of caregivers and professionals to early identify signs of infestation and maintain environmental hygiene (Mohammadi et al., 2024).

Sanitation: Correct management of organic waste and animal carcasses is crucial to reducing the dipteran population (Barnabé et al., 2016; Borja, 2003).

Vector Control: Proper removal of garbage and animal carcasses; sterile insect release techniques (SIT) have been effective in eradicating species such as C. hominivorax in extensive regions (Hall et al., 2016; Borja, 2003).The Sterile Insect Technique (SIT), which releases males sterilized by gamma radiation, eradicated C. hominivorax from North and Central America, although it is still not widely applied in South America due to high cost (Borja, 2003; Souza et al., 2025).

CONCLUSION

Human myiasis represents a complex challenge that transcends a simple parasitic infestation, revealing itself as a phenomenon of profound interface between biology, medicine, and social reality. Throughout this chapter, we observed that although dipteran larvae are frequently associated with conditions of neglect and precariousness, their understanding requires a vigilant and multidisciplinary approach. The biological duality of these larvae is fascinating and, at the same time, alarming: while some species can cause severe tissue destruction and even host death, others, when used under rigorous scientific control in larval therapy, become valuable tools in the treatment of difficult-to-heal chronic wounds.

The social dimension of myiasis cannot be underestimated. It acts as a silent marker of vulnerability, predominantly affecting individuals in situations of poverty, the elderly, or incapacitated patients. We must recognize that confronting this condition requires more than clinical protocols of mechanical or pharmacological removal; it requires effective public policies for basic sanitation, health education, and a strengthening of the palliative and home care network. The application of forensic entomology in the diagnosis of omission of care highlights the role of science as an instrument of justice, transforming the insect's life cycle into physical evidence of wounded human dignity. Ultimately, prevention remains the most ethical and effective path. The implementation of simple measures, such as rigorous wound hygiene and vector population control, has the potential to mitigate the devastating impact of myiasis. It is expected that this chapter will not only inform on the technical and biological aspects of the pathology but also awaken in health professionals a keen sensitivity to early identification of risk signs.

The future of human myiasis management lies in the integration of academic knowledge with humanized practice, ensuring that scientific advancement effectively translates into protection and care for the most neglected populations.

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