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Polycystic Ovary Syndrome: Clinical Presentation, Diagnostic Challenges, and Evolving Management Approaches

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Abstract: ***Polycystic ovary syndrome (PCOS) is a prevalent and complex endocrine disorder affecting individuals of reproductive age, characterized by ovulatory dysfunction, hyperandrogenism, and metabolic disturbances. Its pathophysiology involves genetic susceptibility, insulin resistance, inflammation, and hormonal imbalance. The condition leads to reproductive challenges, dermatological concerns, psychological burden, and long term risks including type II diabetes and cardio-vascular disease. Diagnostic criteria have evolved, with the Rotterdam criteria remaining the most widely used for adults. Management focuses on lifestyle interventions, dietary strategies, and pharmacotherapy tailored to patient needs. Early detection and holistic care are essential to improve long-term health outcomes.***
Keywords: PCOS; reproductive-age health; ovulation irregularities; insulin resistance; chronic inflammation; dermatological symptoms; psychological well-being; long-term metabolic risks; type 2 diabetes risk; cardiovascular complications; diagnostic standards; Rotterdam diagnostic criteria; lifestyle and diet therapy.

I. INTRODUCTION

PCOS is a multifaceted hormonal condition that impacts individuals during their reproductive years and is recognized by irregular ovulation, elevated androgen levels, and the presence of multiple ovarian cysts. It stands frequently occurring endocrine conditions in women, affecting approximately 6% to 20% of the population, with the rate differing based on the diagnostic standards used.. The complicated relationship driven by genetics, hormonal, metabolic, and external influences that play a role in PCOS pathophysiology includes insulin resistance and elevated testosterone levels. Long-term metabolic risks like type 2 diabetes mellitus, dyslipidemia, PCOS is linked to an increased risk of cardiovascular disorders and cancer of the endometrium. Clinically, PCOS manifests as irregular menstruation, hirsutism, acne, and infertility.[1]

II. (PCOS): A HISTORICAL OVERVIEW

People with ovaries, especially those who are fertile, suffer from a hormonal condition called polycystic ovarian syndrome (PCOS). Stein and Leventhal initially identified it explicitly in 1935 after seeing women with infertility, cystic ovaries, and irregular periods. Subsequent studies discovered that insulin resistance and hormone imbalances are also associated with PCOS. In 1990, the NIH developed the first set of official PCOS diagnostic criteria. The Rotterdam criteria, which allowed for a more flexible diagnosis, broadened the definition in 2003. International guidelines by 2018 placed a strong emphasis on treating long-term health conditions like diabetes and mental health in addition to fertility. PCOS is now recognized as a complicated illness that requires individualized care and lifetime care.[2]

III. DIAGNOSTIC CRITERIA FOR PCOS

As stated as stated by the National Institute of Child Health and Human Development., PCOS is identified by infrequent or absent ovulation along with physical and/or laboratory evidence of excess androgen levels.[3]

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The National Health Service (NHS) indicates that the diagnostic features of PCOS consist of scans that show polycystic ovaries, high levels of androgenic hormones or symptoms, and irregular or infrequent periods.[4] Additionally, The Rotterdam criteria remain the most commonly applied method for diagnosing PCOS for adults. A PCOS diagnosis would be confirmed by an ultrasound if any two of the following: elevated androgen levels (clinically or through lab tests), irregular ovulation, or the presence of polycystic ovaries were found.[5] During that period, identifying polycystic ovarian structures through ultrasound was considered the "defining feature of PCOS," which was contrary to the prevalent practice in the UK and much of Europe. Findings of ultrasound imaging revealed ovaries with polycystic characteristics noted as a potential indicator of PCOS, though they were not considered definitive for diagnosis.[6]

IV. DISEASE PATHOPHYSIOLOGY

Based on the diagnostic criteria, PCOS affects approximately 8% to 20% of women globally during their reproductive years.[4] The pathophysiology of this disorder involves alterations in development of ovarian follicles, hormone synthesis within the ovaries, neuroendocrine regulatory processes, metabolic functioning, the body's response to insulin, insulin secretion mechanisms, fat tissue function, inflammatory responses, activity of the sympathetic nervous system.[7] Barre et al. suggest that the primary pathophysiological drivers of PCOS is associated with excessive intake of carbohydrates, high insulin levels, elevated androgen production, and persistent low-level infammation.[8]

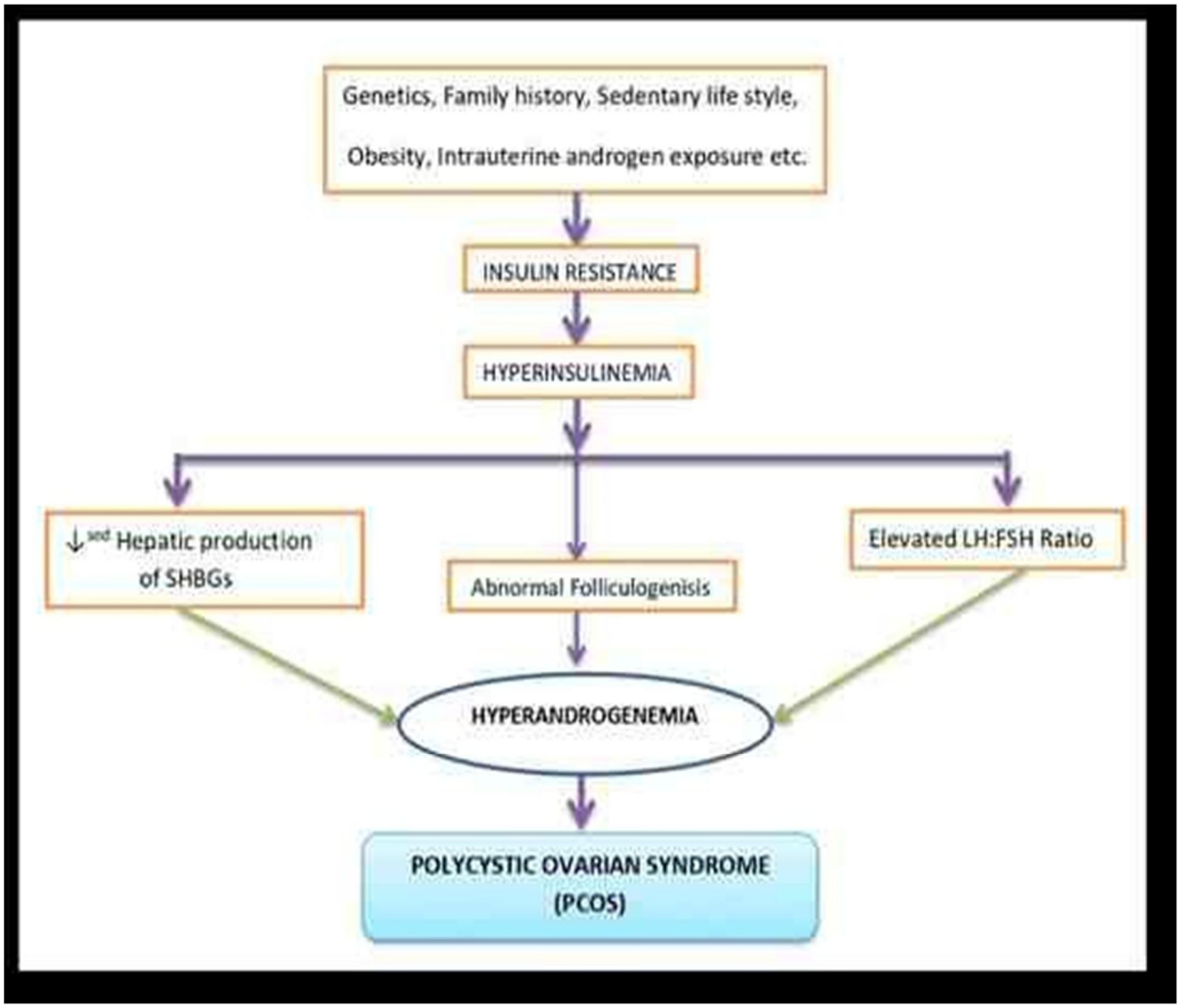


Figure:1 Disease pathophysiology

V. CAUSES AND RISK FACTORS

The intricate and interrelated nature of its pathophysiology makes pinpointing the root causes of this multifaceted disorder challenging. The genesis,the occurrence and expression of PCOS may be affected by gut dysbiosis, genetic factors, environmental contaminants, dietary and lifestyle choices, and obesity.[9] The onset of insulin The metabolic syndrome could be elevated by reduced insulin responsiveness, interruption of normal follicle development, increased ovarian androgen production, and continual low-level secretion of inflammatory substances by immune cells.

VI. CLINICAL SIGNS OF PCOS

A diverse array of clinical manifestations, particularly affecting reproductive, metabolic, and skin-related systems, are present in PCOS.[10] Chronic anovulation causes frequent irregularities in menstruation, such as amenorrhea and oligomenorrhea. Unusual ovulatory cycles are frequently the cause of infertility. A defining characteristic is hyperandrogenism, which can show up as androgenic alopecia, acne, and hirsutism. Biochemically, there may be increased levels of androgens (such as DHEAS and testosterone) in the blood. (PCOM), which is typified by ovaries that are increased in size with a large number of peripheral follicles, is frequently seen on ultrasound.[11] The common Metabolic complications involve reduced insulin sensitivity, abnormal lipid profiles, and a higher likelihood of developing type II diabetes. Symptoms related to metabolism and reproduction are made worse by obesity, especially central adiposity. Low self-esteem, depression, and anxiety are common psychological symptoms that significantly affect quality of life. Obstructive Women with PCOS are more likely to experience sleep apnea and other sleep-related disorders.**[12]** Other possible features include fat accumulation in the liver not caused by alcohol and acanthosis nigricans. Every patient needs to be assessed and treated differently because of the variety of clinical presentations.

VII. OVARY MORPHOLOGY

Ultrasonography has revolutionized diagnostic capabilities in this field since the 1980s by enabling non- invasive evaluation of ovary morphology.[13] As ultrasonography technology advances, follicles can be seen more clearly during ultrasonography due to the increased precision of ultrasonography equipment. The number of follicles found, however, is still dependent on the particular apparatus used. Significantly, serum (AMH) is released by tiny antral follicles seen during US exams.[14] More women are found to meet when AMH serves as a substitute marker for PCOM, a diagnosis of PCOS requires meeting at least two Rotterdam criteria.[15] AMH may act as an effective indicator for identifying polycystic ovarian features in situations where performing transvaginal ultrasounds on large populations is not feasible.[16] Additionally, both AMH concentrations and the number of follicles naturally decrease with age in individuals with or without PCOS. Despite encouraging results, there is a great deal of variation in the study methodologies and diagnostic thresholds set. To guarantee accuracy across various assays, it is imperative to standardize AMH measurement.[17]

VIII. TREATMENT OF PCOS

A. Lifestyle Management

Fifty percent of women with PCOS are obese. Their metabolism, reproductive system, skin health, and mental health may all suffer as a result. The prevalence of obesity among women in At roughly 20% of the total population, Nordic countries typically have lower rates than many other wealthy countries.[18] Even individuals with PCOS who have a normal weight may have metabolic risks and insulin resistance (IR), which may get worse as they put on weight. According to studies, lifestyle modifications like exercise alone or in combination with behavioral strategies, exercise, and diet can help PCOS women's metabolic health, especially when it comes to lipid profiles and central obesity.[19] It is acknowledged that all PCOS women should adopt a healthy lifestyle in order to enhance their Physical health, body structure, lifestyle quality, and weight-management ability.

B. Loss of Weight and Obesity

Globally, obesity is a serious problem that has an impact on economies, society, and health in both wealthy and developing nations.[20] Numerous studies have examined the effectiveness of weight loss strategies in obese women with PCOS. Oral contraceptive pills (OCPs), sibutramine or orlistat, clinical study, or a combination of OCPs and lifestyle intervention were the three treatment arms in which A total of 149 women with PCOS who were overweight were randomly assigned.[21] One group of infertile

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women with PCOS and excess weight received immediate ovulation induction in a secondary analysis of two trials, while the other group underwent delayed treatment after losing weight and changing their lifestyle.[22] Although the main treatment for PCOS is weight loss through diet and exercise, obese women with the condition frequently find it difficult to follow dietary guidelines. Therefore, focused diet-based weight loss initiatives usually result in only modest improvements in metabolic and reproductive outcomes.[23] The Mediterranean diet, or MedDiet, has several well-known health advantages, such as defense against IR-related conditions like obesity, cardiovascular disease, and type 2 diabetes (T2D). In addition to having a balanced protein intake, it is high in fiber, unsaturated fats, vitamins, and antioxidants. Research shows that the MedDiet boosts insulin sensitivity, improves cholesterol status, and supports endothelial performance while lowering oxidative stress (OS) and inflammation, making it a useful approach For treating disorders such as PCOS, which are linked to excess weight and insulin resistance. Through calorie restriction alone, the ketogenic diet (KD) induces therapeutic ketosis and has a short-term positive impact on PCOS outcomes.

C. Diet

The role of diet in controlling People with PCOS often experience decreased sensitivity to insulin. is up for debate. Restricted diets They have demonstrated benefits in enhancing body composition, lowering fasting blood sugar, and reducing insulin resistance. Regardless of weight loss, exercise and customized diet plans Could play a helpful role in PCOS management. However, the ideal diet for PCOS is still unknown.[24] Two dietary practices that increase insulin sensitivity and lower testosterone levels are Consuming several smaller Eating several times a day while making breakfast the largest meal and keeping dinner smaller. This is especially important because many women with PCOS tend to delay their first meals or frequently miss breakfast.[25] International guidelines recommend following The Mediterranean style of eating is widely regarded as one of the healthiest dietary approaches. Key components involve consistent intake of dietary fiber, healthy unsaturated fats, antioxidant-rich foods, and low-glycemic carbohydrates, combined with moderate amounts of animal-based protein.[26] The Mediterranean diet has been demonstrated to be effective in lowering IR-related conditions, including Excess weight, diabetes type 2, reduced cognitive function, and heart-related illnesses, chronic kidney disease, breast cancer, and Fat accumulation in the liver not caused by alcohol use (NAFLD). This diet's ability to Enhance cholesterol levels, boost insulin responsiveness, and support healthier endothelial activity, modulate inflammatory, OS pathways, exhibit antithrombotic and antiatherosclerotic effects is what makes it so effective.[27] The Mediterranean diet serves as an effective lifestyle-based strategy for managing PCOS, as obesity, PCOS, Reduced insulin sensitivity along with persistent, mild inflammation are strongly interconnected.[28] Researchers discovered a negative relationship between the severity of PCOS symptoms and adhering to the MedDiet. Furthermore, hyperandrogenism, IR, and elevated inflammation were linked to an unhealthy diet in PCOS women.[29] An imbalance occurs in people who mostly eat a Western diet, which has low amounts of fruits and vegetables and high levels of meat, sugars, and n-6 (PUFAs). Chronic mucosal inflammation may result from this diet's disruption of the intestinal microbiota and deterioration of the gut epithelial barrier. On the other hand, the Mediterranean diet helps lower inflammation by enhancing intestinal permeability,The balance of gut microbes and the body’s inflammation levels.[30]

D. Ketogenic diet

The keto diet, or KD, emphasizes consuming a lot of fat and significantly reduced carbohydrate intake to reach nutritional ketosis. When it comes to treating refractory epilepsy, its antiepileptic qualities are well known.[31] Through calorie restriction alone, the KD has been demonstrated to induce therapeutic ketosis, which has a positive short-term impact on PCOS outcomes. This The non-pharmacological method improves metabolic and anthropometric profiles and can be used in addition to pharmaceutical treatments for PCOS.[32,33]

E. Drugs

For many women living with PCOS, the initial recommended approach to management do not want to get pregnant is (COCs) and lifestyle changes. They are employed To increase clinical indicators of hyperandrogenism and control the menstrual cycle.[34] While the estradiol component of combined oral contraceptives lowers serum-free androgen levels by increasing SHBG levels, the progestin component suppresses LH secretion, thereby inhibiting the production of ovarian androgens.[34,35] Some progestins inhibit the 5-α reductase enzyme's activity or prevent androgens from attaching to their receptors. Leading clinical Recommendations and

reputable scientific publications, Such as the most recent global guideline for PCOS endorsed by ASRM and ESHRE, recommend (COCs) as the first-line treatment to help adult women with PCOS maintain regular menstrual periods and reduce hyperandrogenic symptoms.[35,36,37] Generally, A dosage ranging from 20 to 30 µg of ethinyl estradiol, or an equivalent amount, is recommended as the minimal effective dose for combined oral contraceptive use. By using this method, metabolic risks and other adverse effects are reduced.[38] The guidelines stress that evaluating the effectiveness of hirsutism treatment must take at least six months. Furthermore, since there is currently no proof that the efficacy of various formulations of combined oral contraceptives differs significantly, no particular preparation is advised over another.[39,40,41] Therefore, we came to the conclusion that combined oral contraceptives and lifestyle changes assist women with PCOS in achieving regular periods and easing symptoms caused by excess androgens.

For sixty years, the pharmaceutical drug metformin has been in use.[42] Additionally, it is a kind of biguanide drug that lowers intestinal absorption, improves insulin sensitivity, and lessens the liver's production of glucose, all of which effectively lower blood sugar levels. Consequently, It reduces blood sugar levels during fasting and after meals. Metformin plays an important role in PCOS treatment by decreasing insulin, which subsequently reduces androgen and LH levels. This normalization of hormone levels plays a role in controlling women's menstrual cycles. Premenopausal women taking metformin should be informed by their clinicians about the increased risk of pregnancy.[40,43]

Clomiphene citrate (CC) is the main drug prescribed to stimulate the induction of ovulation in teenagers who have been diagnosed with PCOS.[44] CC inhibits the hypothalamus's estrogen receptors (anti-estrogen). The anterior pituitary's GnRH pulse width increases as a result of this action, which raises the production of FSH.The medication is administered for a five-day period, typically beginning on cycle day two through day five, starting at 50 mg, with the possibility of increasing the dosage to 150 mg per day For individuals with PCOS who do not achieve ovulation using CC alone, a combination of CC and metformin may be recommended. Around one in five pregnancies can result in miscarriage or stillbirth. despite making up around 30% of successful pregnancies. Potential side effects include hot flashes, gas, ovarian enlargement, fatigue, bloating, multiple pregnancies, and hyperstimulation syndrome.[45,46]

F. FDA APPROVED DRUGS FOR PCOS

Table: 1 FDA APPROVED DRUGS FOR PCOS

Drug Class	Example Drug(s)	Mechanism of Action (MOA)	Common Uses in PCOS	Key Adverse Drug Reactions (ADRs)
Insulin Sensitizer	Metformin	Decreases glucose production by the liver and improves insulin sensitivity in peripheral tissues. This lowers overall insulin levels.	* Regulating menstrual cycles * Improving metabolic health (insulin resistance) * Sometimes used to aid in weight loss * May help with ovulation induction	*Gastrointestinal issues (diarrhea, nausea, gas, bloating) - very common * Vitamin B12 deficiency (with long-term use) * Lactic acidosis (very rare but serious)
Combined Oral Contraceptives (COCPs)	Various (e.g., Ethinyl estradiol + a progestin like Drospirenon or Norgestimate)	* Suppresses ovulation. * Increases sex hormone- binding globulin (SHBG), which binds and reduces free testosterone. * Regulates the	* Regulating menstrual cycles (primary use) * Hirsutism (reducing excess hair growth) * Acne * Endometrial protection (reduces cancer risk)	* Nausea, breast tenderness, headaches * Mood changes * Increased risk of blood clots (VTE) * May affect blood pressure

		endometrium (uterine lining).		
Anti-androgen	Spironolactone	Competitively blocks androgen receptors (like testosterone) in tissues. It also mildly inhibits androgen production.	* Hirsutism (excess facial/body hair) * Acne * Androgenic alopecia (hair loss)	* Hyperkalemia (high potassium levels) * Menstrual irregularities (if not taken with a COCP) * Dizziness, lightheadedness * Breast tenderness * Must not be used in pregnancy (birth defects)
Ovulation Induction	Clomiphene Citrate (Clomid)	Acts as a Selective Estrogen Receptor Modulator (SERM). It blocks estrogen receptors in the hypothalamus, "tricking" the brain into thinking estrogen is low. This increases the release of FSH and LH, which stimulate follicular growth and ovulation.	* **Infertility** (to induce ovulation in women who are anovulatory/olig o-ovulatory)	* Hot flashes * Abdominal bloating/discomfo rt * Mood swings * Visual disturbances (rare) * Risk of multiple pregnancy (e.g., twins)
Ovulation Induction	Letrozole (Femara)	An aromatase inhibitor. It blocks the conversion of androgens to estrogens, lowering overall estrogen levels. This triggers the pituitary gland to release more FSH to stimulate follicular development.	* **Infertility** (to induce ovulation). Often considered first-line over clomiphene for PCOS-related infertility.	* Hot flashes * Fatigue * Dizziness * Joint pain/muscle aches

IX. CONCLUSION

PCOS is a multifactorial disorder with significant implications for reproductive, metabolic, and mental health across the lifespan. Variability in clinical presentation necessitates individualized assessment and treatment guided by current diagnostic standards. Lifestyle modification remains the cornerstone of therapy, supported by pharmacological options such as combined oral contraceptives, insulin-sensitizing agents, and ovulation- induction medications when fertility is desired. Continued research into the mechanisms of PCOS, along with improved diagnostic consistency, is crucial for advancing personalized care and reducing long-term complications.

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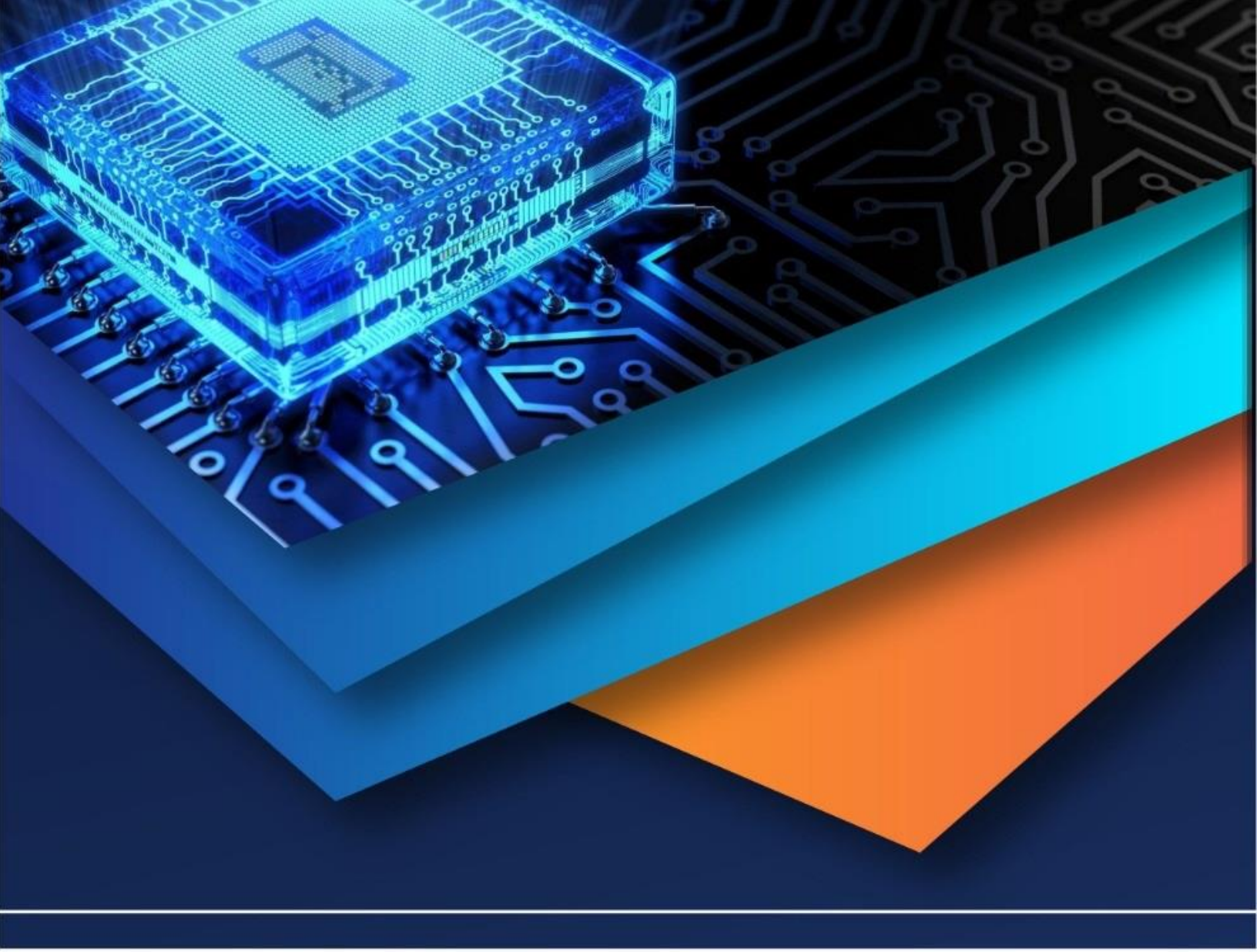
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