Review

Potential use of durian fruit (Durio zibenthinus Linn) as an adjunct to treat infertility in polycystic ovarian syndrome

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ABSTRACT

Infertility due to polycystic ovarian syndrome (PCOS) is a worldwide problem that is increasing at alarming rates. Insulin resistance, the prime factor of PCOS, induces comorbid metabolic syndrome as well. Durian (Durio zibenthinus Linn), a fruit of Southeast Asia, is used as a natural supplement in healthy diets. This paper is a short literature review that examines the fruit’s effects against various components of metabolic syndrome and its fertility-enhancing properties in PCOS. Various published literature was reviewed to learn of the anti-inflammatory, anti-oxidant, anti-obesity, anticholesterol, and antihypoglycaemic nature of the fruit. The literature search was done using PubMed, Google Scholar and library databases. The keywords used were polycystic ovarian syndrome, infertility, metabolic syndrome and Durian zibenthinus Linn. Reviewed studies showed that the fruit is effective against various components of metabolic syndrome, but the mechanisms of action against anovulation and menstrual disturbances in PCOS have yet to be studied. The traditional use of durian as a fertility-enhancing agent needs to be validated scientifically by isolating its various components and ascertaining its fertility enhancing properties.

Keywords: Durian zibenthius Linn; polycystic ovarian syndrome; infertility; metabolic syndrome


1 Introduction

Infertility is defined as inability to conceive after 12 or more months of unprotected intercourse; it commonly affects 13%–15% of couples worldwide[1,2]. Though infertility is categorized as a medical problem, it encompasses various legal, moral and psychosocial issues[3] that often require more complex solutions than typical medical treatment. Studies show that 30%–40% of infertility cases have contributing factors from both sexes[1], and 45% of cases are attributable to the female alone, so understanding the primary causes of female infertility is an important aspect of treating infertility in general[5]. The World Health Organization task force on diagnosis and treatment of infertility performed a study in 8 500 infertile couples to determine the medical conditions contributing to infertility. The most common identifiable female factors in developed countries accounted for 81% of female infertility. These factors included ovulatory disorders (25%), endometriosis (15%), pelvic adhesions (11%), tubal blockage (11%), other tubal abnormalities (11%) and hyperprolactinemia (7%)[3]. Female infertility in the majority of cases results from inability to ovulate, which is primarily due to endocrine disorders, of which
polycystic ovarian syndrome (PCOS) is the main culprit[4]. PCOS accounts for 6% to 10% of infertility cases based on the USA National Institutes of Health criteria[4]. The prevalence rises to about 15% if the broader Rotterdam criteria is applied worldwide[4]. PCOS is an endocrine-metabolic disorder characterized by anovulation, oligo-/amenorrhea, infertility, hyperandrogenism and insulin resistance[5-7], with all above factors being closely interlinked. The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group defined PCOS, in 2004, as the presence of two of following parameters: oligo/anovulation, hyperandrogenism (clinical or biochemical), presence of 12 or more follicles in each ovary measuring 2–9 mm in diameter, and/or an increased ovarian volume (10 mL) with the exclusion of other disorders[9]. Of the approximately 48.5 million cases of infertile women aged 20–44 years worldwide, PCOS accounts for 6%–15%[7]. The deleterious effects of PCOS affect not only female reproductive function, but extend to metabolic syndrome as characterized by abdominal obesity, insulin resistance and dyslipidemias[5,7], which in turn aggravates infertility. As a result, PCOS produces substantial psychological, social and economic consequences[9]. Researchers have described four phenotypes of PCOS based on the Rotterdam criteria that emphasize the clinical manifestations and biochemical context. The primary type includes classical PCOS, with two of three criteria among oligo/anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries. However, the nonclassical type includes women with regular cycles and hyperandrogenism and/or polycystic ovaries[8]. Moreover women with PCOS without clinical evidence of hyperandrogenism, but presenting with ovarian dysfunction, are included in this syndrome. Hence PCOS can be classified as severe PCOS (61%), hyperandrogenism and chronic anovulation (7%), ovulatory PCOS (16%) and mild PCOS (16%)[9].

The therapeutic modalities of PCOS target the anovulatory infertility of PCOS. Anovulatory conditions are usually treated with lifestyle modifications, metformin, antiandrogens, hormones and in-vitro fertilization (IVF)[9]. Lifestyle modifications play a vital role in treatment, and it has been shown that even a 5% reduction in the total body weight, with loss of central fat, will improve insulin sensitization[10,11]. Clomiphene citrate still remains the first choice of ovulation induction therapy even though cheaper aromatase inhibitors are available. However, the teratogenic effects of aromatase inhibitors have yet to be substantiated. The role of metformin and other insulin sensitizers is not primary in ovulation induction, although their role as an adjunct cannot be denied[11]. Metformin has alternatively been found to be a direct inhibitor of ovarian steroidogenesis, apart from being an adjunct in treatment of hyperandrogenism, chronic anovulation and insulin resistance[12,13]. Gonadotropin therapy and laparoscopic ovarian diathermy offer long-term cumulative conception rates[11]. Gonadotropins and surgical modalities are most frequently sought measures for long-lasting benefits, though they have the disadvantages of inducing ovarian hyperstimulation and causing adhesions respectively[9,10].

Durian (Durio zibenthinus Linn) belongs to the family Bombacaceae and features large seeds surrounded by fleshy arils. It is an important native fruit of the Southeast Asian islands. Durian has a characteristic large size, unique odour and formidable thorn-covered husk[19]. It is otherwise known as “king of tropical fruit” owing to its highly nutritious superlative pulp and outer thorny appearance, resembling the thrones of ancient Asian era kings[15,16]. Durian fruit can reach up to 30 cm in length, 15 cm in diameter and can weigh between 1 and 3 kg[16,17]. Durian grows well in warm tropical areas with 75%–80% humidity and is abundantly available from mid-May until July[17]. Though there are 200 different varieties grown, Mon Thong, Chani and Kan Yao varieties are most well-known[18,19]. Durian is used extensively by naturopaths who use it as a traditional treatment of fevers, jaundice and infertility[16,20]. Villagers of southern India use durian for fertility enhancing and consume the fruits available from Nilgris, southern India[20]. The leaves are ground, juice-extracted and applied to the forehead of fever patients in the Malayan Peninsula[16,20]. The ash of the burned rind is given as an oral medicine for postpartum mothers[20]. Though used extensively by naturopaths for fertility issues, we still lack scientific data to prove it. This paper is intended to be a narrative, nonsystematic review based on available evidence, to compile and present the beneficial effects of durian for various aspects of metabolic syndrome, and to suggest its use as a potential fertility enhancer in cases of PCOS with metabolic syndrome. The review was done by employing intensive literature search using PubMed, Google Scholar and library databases. The keywords used were polycystic ovarian syndrome, infertility, metabolic syndrome and Durian zibenthinus Linn.

2 PCOS: pathogenesis of infertility and co-morbidities

2.1 Pathogenesis related to abdominal obesity

Of the various pathophysiological mechanisms noted, abdominal obesity in PCOS women may be co-responsible for the development of hyperandrogenism and the resultant chronic anovulation[21]. The harmful effects of abdominal obesity on female fertility include precocious puberty, menstrual disturbances, risk of miscarriages, worse outcome of deliveries, and metabolic syndrome[22]. The pathophysiological process of obesity resulting in
PCOS has various mechanisms. Obesity in these women induces hyperinsulinism and insulin resistance. Insulin in turn stimulates steroidogenesis and excessive androgen production from the theca cells[21,22]. The high level of insulin induces constant production of luteinizing hormone (LH)[9,23]. Baillargeon and Carpentier[24] reported that insulin contributes to hyperandrogenemia even in lean PCOS women, a finding indicating increased sensitivity of the androgenic insulin pathway in PCOS women. Insulin causes loss of dominance and premature follicular atresia leading to an increased number of follicles[20].

A challenging aspect of obesity-related hyperinsulinemia was raised by Dunaif et al[9], who showed that PCOS women have significant insulin resistance irrespective of obesity, body composition and glucose tolerance. The hyperinsulinemia associated with PCOS is unique. Baillargeon and Nestler[26] have hypothesized that women develop PCOS because of an intrinsic defect that leads to a selective and tissue-specific increase in insulin sensitivity in the ovarian androgenic pathway, independent of LH stimulation. Moreover, ovarian cells of women with PCOS exhibit a higher response to insulin-stimulated androgen synthesis, leading to a cascade of events pertaining to hyperandrogenism[26].

Obesity induces a hyperoestrogenic state, which exerts a positive feedback mechanism on gonadotropin release, and triggers ovarian androgen production; this phenomenon is regarded by Norman et al[9] as uncontrolled steroidogenesis leading to PCOS. The ovaries of these patients secrete abnormal amounts of androgens in response to LH stimulation, and have many antral follicles, both primary and secondary, when compared with healthy ovaries[9]. This is attributed to the direct effect of androgen on ovarian cells, apart from relative follicle-stimulating hormone (FSH) deficiency, abnormal LH stimulus and deficiency of certain local growth factors[9,10]. Follicular stockpiling may be attributed to deficient growth signals from the oocyte and inhibitory effects of excessive anti-Mullerian hormone. Follicular arrest in these women is associated with excessive stimulation of follicular cells by insulin, LH or both[9].

2.2 Other factors leading to fertility disruption in PCOS

Opioids such as β-endorphin were found to be increased in PCOS women, also stimulating insulin secretion. The peptide leptin provides a new insight in considering other possible factors of fertility disrupters in women with PCOS and metabolic syndrome. Leptin directly acts on the ovaries and their receptors, as detected on ovarian follicular cells, granulosa, theca and interstitial cells. High leptin concentrations in the ovary inhibit both granulosa and theca cell steroidogenesis and interfere with follicular development and oocyte maturation[7,21]. Hyperleptinemia increases levels of pro-inflammatory mediators, stimulates chemotaxis of lymphocytes and reduces lymphocyte apoptosis[7].

Current reports correlate both obese and nonobese PCOS with low-grade inflammatory changes. Patients were found to have elevated serum tumor necrosis factor (TNF) and C-reactive protein, high circulating levels of monocyte and lymphocyte and inflammatory changes in ovarian tissue[7]. The circulating inflammatory cells utilize glucose as their substrate and yield nicotinamide adenine dinucleotide phosphate (NADPH). Oxidation of NADPH leads to the production of reactive oxygen species (ROS) that in turn increase levels of pro-inflammatory mediators. This phenomenon marks the beginning of oxidative stress in PCOS women[7].

Another peptide ghrelin, produced mainly in the stomach, is found in low levels in obese women and hypogonadal men. Ghrelin levels are inversely proportional to insulin levels, as evidenced by higher levels of ghrelin of PCOS women who were treated with anti-androgens[21].

Afamin, a vitamin E-binding protein, is found in high concentration in the follicular fluid of PCOS women. Afamin counteracts the anti-oxidant activity of vitamin E in PCOS patients. Afamin induces oxidative stress and inflammation leading to elevated ROS culminating in elevated TNF-α levels secreted from mononuclear cells[27,28]. TNF-α is an indicator of chronic inflammation, proving that ROS-induced oxidative stress aids in development of insulin resistance and hyperandrogenism[18,29].

2.3 Pregnancy-related complications in PCOS

Research has shown an increased frequency of recurrent pregnancy loss in women with insulin resistance and PCOS[30]. This has been attributed to a hostile uterine environment in PCOS women and elevated plasminogen activator inhibitor-1[4,30]. Early pregnancy loss was attributed to LH hypersecretion, which produces a premature oocyte incapable of fertilization or culminates in early miscarriage[4,10]. Fauser et al[4] elaborated that paracrine dysregulation of growth factors disrupts the intrafollicular environment and impairs the maturation of oocytes. The role of periconceptional diets for women with PCOS still needs further exploration[29].

2.4 Dyslipidaemias and related complications in PCOS

Since abdominal obesity and metabolic syndrome are so strongly linked to PCOS, an overview of lipid profile abnormalities in these women is important. Dyslipidaemia is encountered in about 70% of women with PCOS, both obese and nonobese, where obesity aggravates the condition[43,31,32]. These women have low levels of high- density lipoprotein (HDL) and HDL₂. Moreover, there are alterations in the HDL quality
formation in inhibit LDL atherogenic modifications and lipid peroxide oxidants that prevent the rise of plasma lipid levels, and rats have shown that the fruit contains powerful anti-alcoholic extracts of durian to hypercholesteremic fruits of durian are a rich source of soluble fibers that compounds. Polysaccharide gels extracted from the exotic fruits, durian contains high amounts of bioactive proteins, fats, water, ash and fiber supplement durian is an excellent source of carbohydrates, variety, which has higher bioavailability vitamin C found in durian is characteristic of Lisbon sugars, and amino acids including tryptophan. Analysis of apolipoproteins, which regulate the metabolism of lipoproteins and lipid transport, shows that apolipoprotein A-I with cardioprotective effects was lower in women with PCOS. Conversely, apolipoprotein C-I, which increases the postprandial serum lipid levels, is significantly higher in women with PCOS.

3 Active compounds in durian

Durian is rich in vitamins B, C and E and has high iron content. Durian contains a wide array of minerals and trace minerals (Zn, Cu, Mn, Fe, Na, Mg, Ca, K and P), sugars, and amino acids including tryptophan. The vitamin C found in durian is characteristic of Lisbon variety, which has higher bioavailability. As a dietary supplement durian is an excellent source of carbohydrates, proteins, fats, water, ash and fiber. Phytochemical investigatois have isolated a variety of active glycoside, saponins, flavonoids and sterols in the fruit.

4 Durian as an antilipidemic agent

Durian is considered as an “exotic” fruit as its bio-defensive effects are not reachable to majority of the global community yet. As is common in many exotic fruits, durian contains high amounts of bioactive compounds. Polysaccharide gels extracted from the fruits of durian are a rich source of soluble fibers that have laxative properties. Researchers who have fed alcoholic extracts of durian to hypercholesteremaic rats have shown that the fruit contains powerful anti-oxidants that prevent the rise of plasma lipid levels, and inhibit LDL atherogenic modifications and lipid peroxide formation. The polysaccharide gel is additionally able to entrap lipids and aids in control of lipid levels. The durian polysaccharide gel decreased the release of lipids by viscosity-mediated interference on the lipid-releasing outer membrane. Durian is reportedly rich in n-3 fatty acids, which would make it a rich source of polyunsaturated oils, and effective in reducing serum cholesterol. Durian glycaemic index scores were low in comparison with its counterparts. Durian promotes weight reduction by delayed gastric emptying and early satiety due to its low glycaemic index.

5 Anti-oxidant properties of durian

Durian is used in various medicinal formulations owing to its anti-oxidant, antimutagenic, anticarcinogenic, anti-inflammatory and antimicrobial properties of its phenolic compounds. Polyphenols have a strong endothelium-dependent vasodilator activity that prevents nitric oxide degeneration and hence commends them as anti-oxidants. Caffeic acid and quercetin are the dominant anti-oxidants found in the fruit. Quercetin exhibits an extensive range of pharmacological properties and is both the most abundant and most effective flavonoid in human diet. The bioavailability of quercetin is an important consideration. Rapid glycosylation leaves only a small amount of free quercetin available in the blood stream. Rats fed high-cholesterol diets significantly benefited from ripe Mon Thong durian extract, which is rich in quercetin, polyphenols, and phytochemicals that help to reduce damage in the aorta and liver. Durian has been suggested as a vital nutritional supplement, based on its cardio- and hepatoprotective effects, by researchers who conducted studies on laboratory animals. Studies that compared and contrasted Mon Thong, Kan Yao and Chani varieties concluded that the Mon Thong variety has the highest content of bioactive compounds and anti-oxidant capacity. The harmful effects of fibrinogen, leading to a cascade of thromboembolic events, have been substantially reduced by consumption of the fruit. An investigation of the anti-oxidant capacity of ripe durian fruit concluded that the polyphenol content in the ripe fruit was much higher than its tropical counterparts of unripe and overripe fruit. Durian has been shown to be an exotic fruit taking a vital role in disease preventing diets.

6 Durian as a hypoglycaemic agent

Durian has been shown to have hypoglycaemic effects. The fruit improves glucose homeostasis by altering the secretion of insulin and potentiating its action. This was supported by significant improvement of the insulin response curve in diabetic patients after durian ingestion. The antihyperglycaemic function of durian is
due at least in part to its flavonoid composition. The most widely accepted explanation for the antihyperglycaemic function is regeneration and stimulation of the release of insulin by the β cells of the pancreas[38]. Researchers studying the effects of durian in alloxan-induced diabetes mellitus rat models concluded that it exerts antidiabetic actions via different mechanisms: durian directly inhibits glucose absorption and stimulates the release of insulin; its indirect mechanisms include anti-oxidant activity that prevents the glycation and oxidation of glucose to advanced glycogen end products[39].

7 Durian as a fertility booster

Treatment of PCOS-related infertility typically includes drugs such as anti-oestrogens to induce ovulation and insulin sensitizers to address the comorbidities of PCOS[2]. Though the insulin-sensitizing activity of durian has been proven[37,38], its activity against oestrogen has yet to be substantiated[14]. Since adjuncts such as metformin act on ovarian steroidogenesis, hyperandrogenism and anovulation[12,13], investigating these actions of durian would be of great value. Though traditionally the fruit is consumed as a fertility-enhancing agent, researchers have not yet gathered evidence on its fertility-enhancing activities, especially in the case of PCOS[14].

8 Possible role of new insulin sensitizers

Besides the oestrogen receptor modulators, insulin sensitizers and gonadotropins that are available today, alternative medicines are also considered an important adjunct in the pretreatment of anovulatory PCOS. D-chiro-inositol, a dietary supplement of inositol, is an essential component of phospholipids and was found to have promising results in inducing controlled ovarian hyperstimulation when given along with metformin[39]. Inositol is basically an anti-oxidant that improves glucose metabolism, reduces circulating levels of LDL and triglycerides, and also reduces body mass index (BMI)[39]. Laganà et al[40] suggested that D-chiro-inositol was effective in improving the ovarian function and metabolism of patients affected by PCOS. Their study subjects had significant reductions of systolic blood pressure, LH, LH:FSH ratio, total and free testosterone, Δ-4-androstenedione, prolactin levels and HOMA (homeostatic model assessment) index. Moreover, they observed statistically significant posttreatment menstrual cycle regularization.

A study by Genazzani et al[41] focused on PCOS patients with BMI > 26 and treated them with D-chiro-inositol. They found that the pretreatment BMI strongly influences the posttreatment outcome. They also found significant improvement in the biochemical parameters especially in PCOS patients with diabetic relatives. These research findings employing alternative therapy revealed new ways to address infertility and other comorbidities associated with PCOS.

9 Conclusion

PCOS-related infertility is a complex process with insulin resistance as the prime factor that starts a cascade of events leading to metabolic syndrome and infertility. Durian, an exotic fruit of Southeast Asia, has been shown to have anti-oxidant, anti-inflammatory, antihyperglycaemic and anticholesterol effects. Additionally, durian consumption has been linked with weight loss and improvement in metabolic disorders. As a nutritional supplement, durian fruit can address various components of PCOS and associated metabolic syndrome—specifically, insulin resistance, which is the key factor in initiating a cascade of deleterious physiological events. Durian fruit has traditionally been used as a remedy for infertility, but there is no substantive scientific evidence for this use. The lack of robust data on the above hypothesis is a serious limitation. The evidence gathered through this preliminary review will help to enlighten researchers on durian’s ability to address the comorbidities of PCOS. Further research on this topic should include studies on durian’s effects on anovulation (LH, and LH:FSH ratio), menstrual disturbances, inflammatory mediator levels, leptin, ghrelin and afamin levels in PCOS. Studies conducted with D-chiro-inositol showed satisfactory results and they serve as a catalyst to encourage researchers to determine similar results with durian. Promising results may confer this fruit as an imminent component of integrative medicine that can be administered as an adjunct in the holistic treatment of infertility and metabolic syndrome of PCOS.

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11 Competing interests

The author declares no competing interests

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