# Lifestyle disease diabetes and infertility: you caused it, you can cure it; you do not have to die

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#### **Abstract:**

Lifestyle diseases are associated with the manner in which a person or group of people lives. Lifestyle habits have an impact of causing various kinds of communicative and non-communicative diseases including diabetes, infertility, cancer, etc. Due to urbanization, socio economic scenario, stress, lack of proper physical and mental exercise, work pressure changes the systematic rhythm of life which leads to deadly disease. Diabetes and infertility are two most common deadly life style diseases in present day scenario. The causative agent and etiological phenomena of both the diseases are different, but they are highly co-related. High plasma blood glucose level causes diabetes due to lack of insufficient insulin or malfunction of glucose metabolism which often caused obesity. Number of required amount of good quality of sperm, oocyte and other reproductive dysfunctions cause infertility. In this review we have systematically discussed the probable causes of these diseases and provided better solution to reduce these by simple changing the life style.

Keywords: Lifestyle disease, Diabetes, Infertility, Insulin, Glucose, Sperm

### INTRODUCTION

Due to advancement of medicine, treatment procedure, some of the diseases are manageable but a new breed of diseases has recently developed or aggravated called 'lifestyle diseases' that include heart diseases, diabetes, infertility, etc. These deadly diseases are no longer problem just in wealthy nations. Globally 14.2 million people between the ages of 30-69 years die prematurely each year from these diseases. These diseases have emerged as bigger killers than infectious or hereditary ones. The onset of lifestyle diseases usually take years to develop, but once developed do not lend themselves easily to cure. Factors like abuse of alcohol, drug, smoking, lack of physical exercise, unhealthy and excessive eating, stress are linked with the occurrence of these type of diseases [1][2][3]. Diabetes is a disease where enough insulin is not produced or body is unable to use the insulin effectively as a result the blood glucose level raised excessive high. Untreated this disease caused severe health related complications [4]. Diabetes leads to other multiple complications such as obesity, heart diseases, neuropathy and retinopathy which are well discussed in elsewhere.

Infertility is a global problem in mammoth dimension. It is not only a disease but social stigma. The childless couple faces multiple problems not only in family but also in society too. Several lines of report suggest a direct link between diabetes and infertility. In this review we have systematically discussed the cause and concern of most deadly life style diseases diabetes and infertility and correlation between them and finally provided probable solution to reduce the diseases only by changing the life style not by taking medicine.

#### **Diabetes:**

Diabetes mellitus (DM) or commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. The common symptoms of diabetes are increased 3P's, Polyuria (increased urination), Polydipsia (increased thirst), and Polyphagia (increased hunger). If left untreated, diabetes can cause many complications. Acute complications can include

diabetic ketoacidosis, nonketotic hyperosmolar coma, or death. Serious long-term complications include heart disease, stroke, chronic kidney failure, foot ulcers and damage to the eyes.

Blood glucose level is maintained by the antagonistic effect of insulin and glucagon, hormone secreted form the beta and alpha cells of islets of Langerhans of pancreas, respectively. But when the pancreas is unable to secret enough insulin or body is unable to utilize insulin efficiently, glucose that comes from our food stays in our blood and then diabetes comes into picture (Fig.1). When it is uncontrolled, it has direct consequences for health and well-being. Right now diabetes is one of the most important health problem and one of four priority noncommunicable diseases hunting our world. According to WHO, in the year 2014 an estimated 422 million adults having this global burden as compared to 108 million in 1980 [5]. As informed above, its consequences are also havoc. In 2012, 1.5 million deaths were reported due to diabetes and increasing risks of cardiovascular and other diseases due to high blood glucose caused additional 2.2 million deaths. Among this 3.7 million, 43% of deaths occurred before the age of 70 [5]. Though Type I Diabetes Mellitus and Type II Diabetes Mellitus are mainly well-talked, there are other types of diabetes also. Gestational Diabetes, LADA (Latent Autoimmune Diabetes in Adults), MODY (maturityonset diabetes of youth) are among them.

In type I diabetes, sufficient amount of insulin is not being produced and due to lower level of insulin, blood glucose level increases <sup>[6]</sup>. Where type II diabetes is the consequence of long term metabolic disorder and here due to insulin resistance blood glucose level increases <sup>[6]</sup> (Fig.2). According to WHO, type II diabetes has the global scenario of about 90% diabetes and it is

mainly the result of obesity and not enough exercise <sup>[7]</sup>. There is also a term called Diabetes Insipidus where due to lower level of ADH (antidiuretic hormone) or vasopressin, water reabsorption of DCT (distal collecting tubules) reduced; and a result of that excretion of large amount of urine occurs (polyuria) <sup>[8]</sup>.

According to WHO, the cause of diabetes type I or IDDM (insulin-dependent-diabetes-mellitus) is still unknown [7], where Knip M et al., shows that environmental factors, genetic susceptibility, exposure to antigen triggers the occurrence of type I diabetes mellitus [9]. Type I diabetes has a high link with heredity. There is about 5% chance of a child developing type I diabetes if the father has it, 8% chance if a sibling has it, about 3% chance of developing this if the mother has it [10] and 50% chance of an identical twin developing type I diabetes if the other has it [11]. Recent study shows that type I diabetes is the early symptom indicating the  $\beta$ -cell autoimmunity, the disease is mostly diagnosed in early ages and due to autoantibody against insulin, glutamic acid dehydrogenase or both [12]. Greater the β-cell autoantibodies, greater the risk of developing diabetes. As discussed earlier, the β-cell autoimmunity has an hereditary relationship, mainly occurring individuals having either HLA-DR3-DQ2 or HLA-DR4-DQ8 haplotypes, or both and it is triggered by environmental factors also [11]. There are more than 50 genes that are involved with type I diabetes and among them the strongest gene is IDDM1, located in the MHC Class II region on the small arm of 6<sup>th</sup> chromosome (6p21) [12][13]. On the other hand, DeLisa Fairweather et al., proposed that in type I diabetes the autoimmune response is triggered by virus and here the immune system attacks beta cells of pancreas also in order to kill the virus-infected cells [14][15].

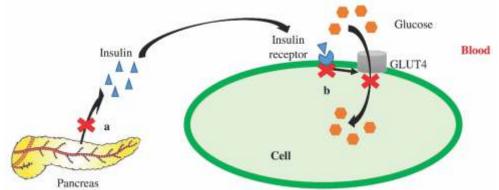


Fig 1: Diagrammatic representation of the action of insulin in glucose uptake from the blood. In normal condition, insulin is secreted from the  $\beta$ -cell of islets of Langerhans of pancreas and binds to insulin receptor. After binding of insulin to its receptor, by signal transduction glucose is up taken by the cell through GLUT4 (after the translocation of GLUT4 to the surface of the cell). In case (a), insulin is not or very less secreted from pancreas and hence the followed procedure wouldn't occur and this leads to Type I Diabetes. Where in (b),

insulin is enough produced but the body has a resistance towards it and hence glucose is not going to uptake from the blood; and this forms Type II Diabetes. In both the cases the blood glucose level increases.

Additionally, lifestyle and genetic factors have the major contribution in type II diabetes mellitus or NIDDM (non-insulin-dependent-diabetes-mellitus) [16]. Here some of the factors are under personal control like diet, obesity and some are not like age, sex and

genetics <sup>[18]</sup>. Sleep deprivation, lack of physical exercise, stress, poor diet can lead to the development of type II diabetes <sup>[18]</sup> [<sup>19]</sup>. According to Herder C *et al.*, there are more than 36 genes that are linked to diabetes type II <sup>[20]</sup>. Here the contributing main gene is NIDDM1 of chromosome 2 (2q37) <sup>[21]</sup>.

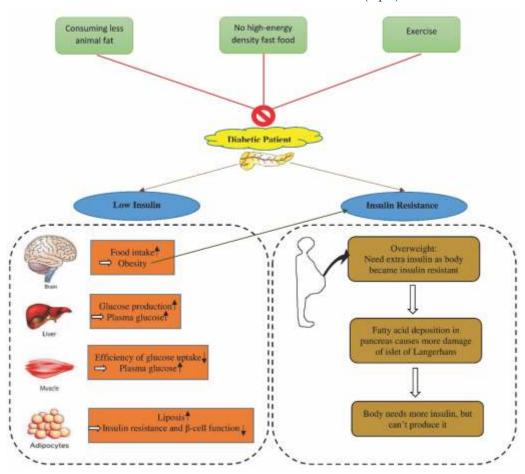


Fig 2: Schematic diagram represents how insulin plays the driving role in diabetic patients. Both in low insulin (Type I Diabetes) and insulin resistance (Type II Diabetes) have a huge consequence on the body. Proper exercise, less fast food intake or consuming less animal fat can retrieve normal insulin level and counteract diabetes.

## Infertility:

Infertility is a term which indicates the inability of an individual to conceive after having regular unprotected sexual intercourse. Infertility was traditionally thought to be female's problem, but as time goes on male infertility comes into picture. Infertility is now a stressful and heartbreaking situation. It is estimated that one in ten couples are facing primary or secondary infertility [22] and in developed and developing country, specialized investigation or treatment is required in one in six couples to conceive [23]. Here primary infertility defines

the inability to conceive who has been union for at least five years without taking any contraceptives <sup>[24]</sup>. However, infertile couple often faced social, cultural and even marital issues and sometimes isolated from fertile world due to social unacceptability and no empathy from family and friends <sup>[25]</sup>.

Male infertility accounts 40-50% of whole infertility in case of human <sup>[26]</sup>. Here male infertility refers to the inability of a man to cause pregnancy of a fertile female. Successful male fertility refers normal spermatogenesis (process of formation of sperms), spermiogenesis (process from which mature sperm or

spermatozoa is formed from immature sperm or spermatid), spermiation (process in which spermatids are released into the seminiferous tubule from Sertoli cells), normal sperm transport and normal accessory gland function [27]. In addition to this, to be fertile, a man should have enough sperm in his semen and those sperm should be healthy. Deficiency of semen and semen quality are the major contributor of male infertility. Swan et al., shows that the sperm count in human declined over the past 50 years simultaneously [28]. Spermatogenesis is initiated during puberty and maintained throughout the life of a normal man. However this spermatogenic process is vulnerable to the adverse effects of changing of healthy lifestyle, exposure of toxic materials and other factors. This male infertility has a huge emotional, physiological impact on male. Infertility leads to sexual dysfunction and thus associated with high level of stigma, low sexual satisfaction.

The present scenario demonstrates that 10-15% couples are infertile and half of the whole infertility case is governed by female infertility factors [29]. Chandra *et al.*, stated that 7.3 million of American women (i.e. 12% of American women population) having infertility problem that they are unable to conceive or carry pregnancy [30]. Being overweight, low or no exercising, cigarette smoking, consumption of alcohol and caffeine are some life style factors which have a major impact in faulty reproduction function in female. Menstrual dysfunction is the leading contributor of female infertility, but apart from that polycystic ovary syndrome (PCOS) is the emerging consequence of female infertility. Fig.3 demonstrate the normal procedure for infertility.

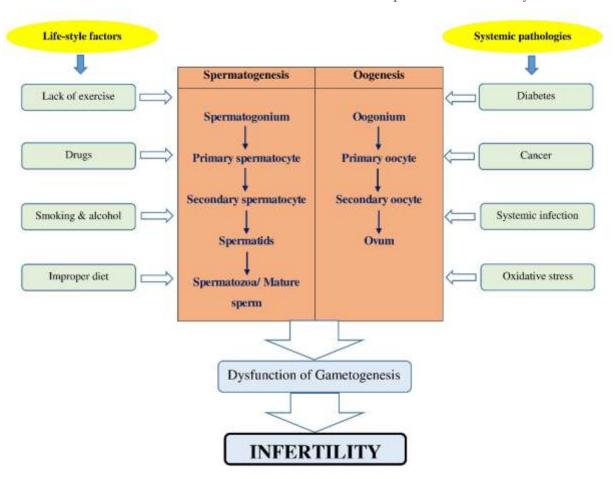


Fig 3: Schematic diagram showing the impact of lifestyle factors and systemic pathologies on the gametogenesis process. Gametogenesis process in both male and female is affected by the above mentioned factors, which leads to infertility.

#### Diabetes, Obesity and Infertility:

As we discussed above diabetes is a disease due to hyperglycemia (blood glucose level is high; normal level is 80-120mg/dl). When we take food, the glucose

is metabolized by various biochemical processes. But in case of some metabolic disorders, consuming greater energy density foods or drinks (irrespective of protein and fat content), excess glucose is converted to fatty

acids in mainly adipose tissue by a process called lipogenesis. Fatty acid synthesis starts with acetyl-CoA, which is the first product of Krebs cycle. Even though, insulin helps to maintain the body glucose level; it also stimulates lipogenesis by activating two enzymatic pathway. At the very beginning of Krebs cycle, acetyl-CoA is formed from pyruvate by Pyruvate dehydrogenase and then acetyl-CoA carboxylase converts acetyl-CoA to malonyl-CoA and then malonyl-CoA provides the two-carbon building blocks that are used to create larger fatty acids. Lipogenesis includes both the fatty acid synthesis and triglyceride synthesis and these products are secreted from the liver in VLDL (very low density lipoprotein) form. These VLDL particles directly secreted into blood and there they mature and endogenously deliver lipids to peripheral tissues. So, devouring more and more fast food, junk foods having high sugar content leads to the formation of being obese; and hence this unhealthy lifestyle gives rise to obesity or diabetes.

There are few definitive studies that prove the relationship between lifestyle factors, diabetes and male infertility. However diabetes mellitus has a significant impact on male infertility in direct and indirect manner. Recent study revealed a high prevalence of infertility in men having diabetes mellitus. Shaban *et al.*, confirmed that 32% of men with diabetes mellitus having some degree of ejaculatory dysfunction and this represents the common cause of infertility in men [31]. It affects the male reproductive function and as a result the endocrine control of spermatogenesis or even spermatogenesis itself got harmed [32].

Diabetic men have a higher levels of DNA damage to their sperm, which leads to infertility and numerous reports demonstrated an increase level of sperm DNA damage in infertile men [33] [34] [35]. Diabetes Mellitus is a recognizable cause of male sexual dysfunction and a recent study strongly demonstrates that rising rate of diabetes may well pose significant hazard to human fertility [36]. Study done by Delfino et al., shows that diabetes mellitus has a negative impact in both sperm quality and ejaculation mechanism [37]. Andy Petroianu et al., believed that diabetes mellitus is associated with male infertility like impotence, ejaculation disorder and even decreased libido [38]. Dinulovic et al., showed that diabetes leads to the changes of Leydig cells which is associated with male infertility due to inappropriate synthesis of testosterone [39]. Miralles-Garcia et al. found that type II diabetes is associated with reduced ejaculation, viability and motility of mature sperm [40].

In the other hand, infertility has a great relationship with the age group of diabetic men. Zheng *et al.*, reported that frequency of impotence due to diabetes is increasing with increasing age [41]. Several studies have shown up to a conclusion that up to threefold increase case of infertility cases are found in obese men than of normal men [42] [43]. Men having BMI>25 is associated with an average 25% decreased sperm count and sperm motility [44].

In addition to this, Padron et al., conclude with the fact that semen volume, sperm motility and morphology were notably lower in diabetic patients [69]. Here all sperm parameters and seminal fructose were lower in diabetic patients. In vivo animal studies also suggest that diabetes alters and significantly compromises male fertility. Among them a study done by Seethalakshmi et al., on streptozotocin (STZchemical toxic to insulin producing beta cells) in rat model and it suggests that diabetes resulted in reduced sperm counts, motility and insulin treatment restored sperm counts, motility [70]. Soudamani et al., also evaluated the effects of STZ-induced diabetes and later insulin replacement on the histologic features of caput, corpus, and caudal epididymis during the period of sexual maturation in rats [71]. Another study explored the outcome of short-term hyperglycemia on epididymal sperm quantity, quality and transit time using both natural mating and artificial intrauterine insemination protocol in STZ-diabetic male rats [72]. Here also diabetes resulted in diminished sperm count within testis and epididymis.

Though the exact mechanism of sperm damage is still unknown, two dysfunctional mechanism can be postulated to explain the damage in sperm observed in diabetic patients: endocrine disorders and oxidative stress. Seethalakshmi et al., conducted an experiment by making diabetic rat and then they were treated with insulin and/or testosterone [70]. A remarkable decrease in serum LH (luteinizing hormone), FSH (follicle stimulating hormone) and testosterone was observed. After insulin treatment, the compromised gonadotropin level was restored. The result of GnRH (gonadotropin releasing hormone) stimulating test also showed that the pituitary gland of diabetic animals has a blunted response with reduced LH and FSH secretion. Another study conducted by Anderson et al., on male Wistar diabetic rats (STZ-treated) exhibited a significantly lower serum testosterone level with high blood glucose and serum creatinine compared with controls [73]. Jelodar et al., also concluded with the fact that significant increase in blood glucose

has a consequence of diminished serum levels of LH, FSH and testosterone level in the offspring of the diabetic mothers [74]. Hence it can be concluded that in insulin-dependent diabetes, Leydig cell function and testosterone level diminished due the absence of stimulatory effect of insulin on these cells. Here also decreased level of FSH leads to the decreased LH level; and sperm output and fertility reduced because of the decreased FSH level. Secondly, oxidative stress can be a major contributor in diabetes related male reproductive function abnormalities. Amaral et al., evaluated lipid peroxidation, protein oxidation, lactate levels, adenine nucleotides, adenylate energy charge, and activity of glutathione peroxidase, glutathione reductase and lactate dehydrogenase in isolated testicular cells [75]. It was observed that sperm motility and concentration were decreased in 3 months STZtreated rats. ATP (Adenosine triphosphate) level also decreased in those rats. However, lipid peroxidation increased after 1 week and 3 months of treatment; glutathione reductase activity was found to be increased. Sandro La Vignera et al., evaluated that diabetes is associated with increased sperm radical oxygen species production which causes male accessory gland infections [76]. All of these data suggest that diabetes is associated with increased oxidative stress and this results in sperm DNA damage and faulty reproductive function. These data also revel the importance of evaluating oxygen radical species production in all diabetic male especially those with infertility.

According to NIH, 35.5% women in USA are obese. Steppan et al., reported the hormone resistin (for resistance to insulin), which secreted from adipocytes, plays as a bridge between obesity and diabetes [45]. Obesity is linked with insulin resistant, in which androgen production is stimulated from ovary and hence in the periphery, androgen aromatization increases. This leads to the alteration of the development of follicles within the ovaries of obese women [46]. An obese woman having pre-pregnancy BMI (Basal Metabolic Index) >24 is highly susceptible to gestational diabetes mellitus and other reproductive pathologies like preeclampsia, pre-term labor [47]. It is also related with decreased pregnancy rate and increased risks of loss of pregnancy. Recent systematic studies stated a clear relationship between occurrences of early miscarriage or decreased in pregnancy rate with obese women having higher BMI [48] [49]. It is also associated with compromised oocyte and embryo quality and it negatively affects the endometrium,

resulting miscarriage due to poor implantation [50]. It has a profound effect on both pathophysiological and clinical manifestation of PCOS [51]. Obesity is believed to interrupt ovarian function, increasing insulin resistance and raising free androgens [65] [66]. These insulin resistance and hyperandrogenism has a significant footprint on PCOS, which may represent an extreme prevalence of ovulatory infertility [67] [68]. Another study done by Ramlau-Hansen *et al.*, stated that obsessed-mother having high BMI has a negative effect on her son's semen quality and reduces Sertoli cell number [52]. Apart from that, it has a severe effect on IVF treatment also. The pregnancy rate decreased half time in case of an obese woman comparing with normal weight woman [53].

Like male infertility, oxidative stress also has a great impact on female infertility especially on oocyte and embryo quality, apoptosis, permanent meiosis arrest, age-related defects and chromosomal abnormalities. The excess production of reactive oxygen species (ROS) in oocyte and embryo can affect mitochondrial function, leading to oxidative stress induced arrest of cell division and cell death; resulting in female miscarriage and infertility [78]. In the mouse model, Liu *et al.*, found that  $H_2O_2$  treatment induced apoptosis in zygotes [78]. So, oxidative stress resulted in increased ROS and decreased antioxidant capacity, has a major role in the etiology of both male and female infertility.

#### TREATMENT:

Diabetes is now-a-days a part of our family and to diagnose this is not a critical issue. Normal blood glucose level and glycosylated Hb check are sufficient enough to check a person having diabetes or not; and sometimes urine glucose level also be checked if blood glucose level is very high (above 180mg/dl). Till now there is no way to prevent type I diabetes; and if people don't keep this in control, serious health-hazard and life-threating problem arises. Many people with type I diabetes spending long and healthy life with proper diet; and having insulin in appropriate proportion depending upon the onset and under regular and proper medical supervision. In addition to this, in some cases pancreas transplantation or islet cell transplantation also work, but they are very consequential process and in these cases HLA matching and immunosuppression is required in order to prevent organ or tissue rejection. People with type II diabetes also can effectively manage it by under regular medical attention and checking blood sugar in a regular time interval. Here the main aim is to keep the

blood glucose level in normal range. In type II diabetes, not everyone needs insulin, but some people do need this because in those cases insulin is not enough produced. Several anti-diabetic medications are readily available in order to keep blood-glucose level in specific level. These classes of medications include metformin, sulfonylureas, dipeptidyl peptidase-4 inhibitors, thiazolidinediones, SGLT inhibitors, glucagon-like peptide-1 analogs, etc.

The necessity of reproduction is the some fact which both Darwin and the Bible agreed. Not being able to be a father or mother, makes a man or woman feel that he or she is failing at one of their most primal responsibilities. To treat infertility, diagnosis is the first step, but unfortunately diagnosis of infertility at very beginning is one of the hardest challenges one can face. Common test to diagnose male infertility is to perform semen analysis. By this, oligospermia, azoospermia, aspermia, hypospermia can be diagnosed. By performing blood test, one can reveal the genetic cause of infertility, e.g. klinefelter syndrome, cystic fibrosis. Ultrasonography of scrotum can detect the sign of testicular dysgenesis and it is also helpful to detect PCOS in female. Apart from these, hormonal test during menstrual cycle, endometrial biopsy, fertiloscopy also can be used to diagnose female infertility.

Treatment of curing male and female infertility is not well studied, but some treatments are currently available to manage the situation. Men infertility due to hypogonadotropic hypogonadism can be treated with LH (Luteinizing hormone) and FSH (follicle stimulating hormone) [54]. There are also some drugs available in the market which is helpful for PCOS and reducing some symptoms; but they can't treat it properly. In the extreme cases when treatment fails or doesn't have any effect on resolving infertility problem, high-throughput techniques like IUI (intrauterine insemination), IVF (in vitro fertilization), ICSI (intracytoplasmic sperm injection) can be used; but here the success rate is also very low and these are also very susceptible to age, obesity and other lifestyle factors.

#### **NOVEL APPROACHES FOR PREVENTION:**

There are above mentioned cumulative evidences discussed in this review that suggests that lifestyle factors such as overweight, high BMI has a great relationship with diabetes and infertility. Hence, lifestyle modification can be the most effective way to counteract these negative consequences in order to improve fertility potential of both male and female. As

we discussed above, obesity and physical inactivity has a tremendous impact on developing type II diabetes followed by infertility; however these factors are modifiable and can be amenable to exercise. Rapid changes of glucose concentration in blood can be occurred due to exercise. Both in type I and type II diabetes, the importance of physical exercise cannot be ignored [55]. Blood glucose level reduced during or after regular exercise through increased glucose transportation from blood to working muscles by insulin-dependent or insulin-independent manner [56]. Hayashi et al., showed that exercise increases the translocation of GLUT4 (Glucose transporter type 4) to the surface of muscle cells [57]. On the other hand researchers showed the presence of two distinct GLUT4 on the surface of skeletal muscle, one corresponding to exercise and another is for insulin [58] [59]. Muscle contraction during exercise, activated AMPK (Adenosine monophosphate protein kinase) produces the translocation of GLUT4 by either insulinindependent [60] or insulin-dependent [61] pools. Hence exercise can be an effective therapeutic tool to prevent and control diabetes in order to get rid of infertility in both male and female.

Apart from this, children and young adolescents haven't developed any cognitive dietary restriction and they are inclined towards high energy density fast foods. The current scenario is like that fast foods are making a great contribution to excess calories consumption and these lead the modern generation highly vulnerable and susceptible to generate diabetes due to long-term weight gain or diabetes in later. Research has been demonstrated that obesity is linked with excess soft drink consumption [62] [63], high saturated fat, low fiber, high salt content of snacks and fast foods [64]. So we have to broaden our limited knowledge and should have a healthy diet to overcome this situation and hence lifestyle modification is must.

In addition to this, antioxidant therapy can be effective against increased sperm radical oxygen species production in order to diminish the occurring of male accessory gland infections. Mohasseb *et al.*, appraised the role of antioxidant supplementation (mixture of vitamin E, C and α-lipoic acid) on testicular germ cell apoptosis of STZ-induced diabetic rats [77]. Hence these antioxidants can be used to reduce germ cell apoptosis, decrease sperm abnormalities (especially morphologic alteration) and improve conventional sperm parameters. Administration of antioxidant significantly improved the imbalance between ROS and antioxidant defenses observed in

infertile women <sup>[79]</sup>. Here the clinical trial of improving nutraceuticals (contains antioxidants CoQ10, astaxanthin, anthocyanidines, essential omega-3 fatty acids, zinc, folic acid, in combination with fish oil), improve the probability of conception and successful pregnancy. Both the clinical and experimental data suggest that the modern lifestyle has a huge impact on developing diabetes and infertility; and hence lifestyle

modification, intense workout, consuming less fast food can be the first course of treatment to improve fertility potential. Antioxidants and other supplements may confer additional benefits by further scavenging ROS. Lastly, assisted reproductive technology can be considered only if less extreme, minimally invasive methods are unsuccessful.

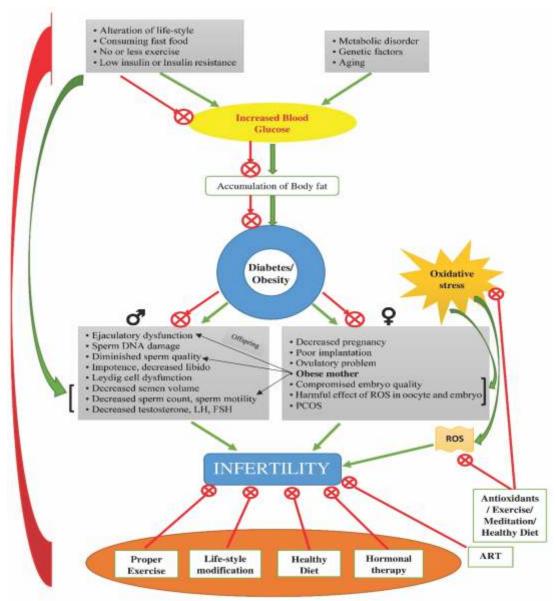


Fig 4: Schematic representation showing the linkage between lifestyle factors and diabetes which is linked with infertility. Modification of daily lifestyle can recover the proper body physiology.

#### **DISCUSSIONS:**

The modern lifestyle, characterized by high energy density fast foods, is taking its toll on children as well as adults and a consequence of this an increased numbers of obese and even infertile youngsters are coming into our consideration. Literature study revealed that

lifestyle factors such as overweight, little or no physical activity, high BMI, consuming more junk foods are detrimental to both natural and assisted fertility in both male and female. Therefore, lifestyle modification such as healthy diet, efficient exercise may be the most effective manner to overcome these negative effects

and to improve and maximize the fertility potential of this modern generation. In addition to that, it is also optimal to execute lifestyle changes before undergoing assisted reproductive techniques (ART), in order to attenuate the negative outcomes and improve the chances of achieving pregnancy and having a child. However, ART may no longer even necessary to those women who had underlaid the causes of infertility and improved their natural fertility potential by creating a habit of modifying those lifestyle factors. But in some cases, it would be better to proceed with ART (mainly when the age of woman is the great concern), than delaying these procedures in order to first implement changes of lifestyle. Various studies have demonstrated the usefulness of lifestyle modification, especially in diabetes and infertility; and hence it is thought to be an effective therapeutic option for those experiencing these lifestyle diseases. Ultimately, although changing in lifestyle appeared to be a protective tool for fertility and a possible avenue for the curing of infertility, future research should be done and should elucidate the duration to get the benefits or to recover from the faulty reproductive function.

## **CONCLUSION:**

Due to urbanization, the life style of people are changing very rapidly. People are now migrating very frequently from one place to others for multiple reasons such as climate changes, natural calamity, job security, earning, educational purpose and so called better livelihood. Due to changes of places and environment, multiple factors such as genetic makeup, adaptability, microbial load of particular region, etc has also changed which create problem in physically and mentally; and ultimately caused diseases (Fig.4). Easily available cooked junk food, less exercise, excessive stress in work place, intake of alcohol, smoking habit and pollution may lead multiple diseases. Diabetes and infertility are such type of diseases. There is a debate between the co-relation of these diseases and more systematic study will be needed to finalize the conclusion. But it is often seen that diabetic people are very prone to infertility. We can reduce the diseases by simple changing the lifestyle we lead. Taking proper healthy food, doing regular exercise, less stress, proper sleep, leaving the smoking and alcohol habit, etc will may changes the scenario (Fig 4). The several literatures over the years and religion Epic suggested beautiful pathways to live the life in the society without hampering the nature. The most of the life style diseases caused by us due to the changes in the way of life. Thus it can be curable by us only by simple changing the life style.

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