



## Paternal Factors and Yoga to the Rescue of Early Pregnancy Loss

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### Editorial

Early Pregnancy Loss (EPL), the loss of non-viable intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without fetal cardiac activity occurs within the first 12 weeks of gestation [1,2]. EPL is seen to occur in 10% of all clinical pregnancies and almost 80% of the same occur within the first trimester [3]. The assumption that pregnancy loss occurs because of maternal rejection of normal embryos is challenged with growing evidences on abnormal quality embryos, immunological incompetence and studies on endometrial receptivity. Impaired embryonic development has been attributed to paternal contributions which are ignored at large. The defects in sperm chromatin integrity, mitochondrial dysfunction and associated oxidative stress, nuclear and mitochondrial DNA damage and dysregulated gene expression have been implicated as to developmental incompetence, pregnancy loss and adverse embryonic and congenital fetal defects and increased incidence of genetic and epigenetic/ imprinting defects [4-7].

Overwhelming stress and anxiety, the contributors of many complex “lifestyle related” chronic diseases such as depression, heart diseases and diabetes, have been implicated as one of the causative factors in various reproductive disorders like infertility, early and recurrent pregnancy loss, congenital malformations due to alarming effects on the health of the future progeny. The effects are adverse due to decrease in quality of life and poor response to pharmacologic treatment. The impact of antioxidant on nuclear DNA damage is still controversial. Efforts are underway to find non-pharmacologic therapies to relieve stress and anxiety, and adoption of yoga as an integral part of our lifestyle is a promising beneficial treatment modality. Yoga, the ancient Indian discipline, is aimed at achieving union and harmony between our mind, body, and soul and brings balance to all aspects of one’s being. It is a highly advanced technique for attaining perfect alignment of body and prepares it for meditation. Evaluation of the current primary literature is positively suggestive of the benefits of Yoga and Meditation based Lifestyle Intervention (YBLI) in relieving stress and anxiety. Yoga causes a down regulation of HPA axis which had been affected by a trigger (stressor) leading to a cascade of physiological, behavioral and psychological effects due to the release of cortisol and catecholamine [8,9]. YBLI has been shown to decrease the levels of cortisol and epinephrine and up regulating the levels of anti-inflammatory genes, cytokines, endorphins and also improves cardiovascular tone [10,11].

YBLI have been observed to decrease OS, DNA fragmentation and lower mutagenic load in the sperm DNA, thus therapeutic for seminal OS and oxidative DNA damage [10,12,13]. Previous studies conducted in our laboratory have shown a decline in seminal ROS levels within 10 days of regular practice of yoga [13,14]. A reduction in ODD had been documented in the spermatozoa over a period of 6 months by adopting simple YBLI [13]. Though the improvement in sperm DNA integrity and decline in the levels of mutagenic base adducts in DNA took nearly 6 months, it becomes all the more important to make YBLI an integral part of lifestyle. OS preferentially targets the telomeres, causes its rapid attrition and thus predisposes to loss of chromosomal stability and increase incidence of complex chromosomal rearrangements and aneuploidies. Thus as yoga causes decrease in OS and up regulation in activity of telomerase it aids in maintenance of genomic integrity. This finding is highly relevant because though genetic causes of infertility, RSA and congenital malformations are irreversible but OS and ODD can be minimized by adopting a healthy lifestyle. Increasing ODD is the chief causes of rapid telomere attrition, accelerated testicular aging and genomic instability. YBLI has been shown to exert a beneficial effect by up regulating the telomerase activity along with a decrease in OS and ODD [15].

The critical changes occurring in pre implantation embryonic development witnesses remarkable changes in the gene expression profile and also associated with marked chromatin

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reorganization and histone modifications (methylation, acetylation, phosphorylation, ubiquitylation and sumoylation). Packaging of sperm nuclear chromatin in spermatozoa at fertilization has a potential role in transmitting an epigenetic profile to the zygote in early embryonic development. The nucleosome retention takes place in hypomethylated regions which corresponds to the promoters of developmental transcription and signaling factors which are the target of transcription factors [16-18].

OS affects the sperm by inducing genome-wide hypomethylation. The accumulation of oxidized mutagenic base adduct 8-OHdG also affects sperm epigenome by inhibiting the methylation of cytosine at CpG islands thus leading to genomic instability due to unmasking of repetitive elements and over expression of oncogenes. OS, accumulation of lipid aldehydes, mitochondrial dysfunction, shorter telomere length and accumulation of 8-OHdG and aberrant methylation are the prime factors contributing to genome instability, accelerated testicular aging and dysregulation in sperm transcripts [10,11,13,19]. Ongoing study from our own laboratory has shown the normalization of gene expression to that of healthy fertile controls in the genes critical for early embryonic development in the spermatozoa. Also the impact of YBLI witnessed a positive change in the expression of the genes of the Base Excision Repair (BER) pathway i.e; OGG1 and PARP1 in the sperm [13,20].

YBLI exerts its affects by two independent epigenetic pathways. The 'direct epigenetic pathway' exerts its effect by affecting epigenetic enzymes i.e; DNA Methyltransferases (DNMTs), Histone Methyltransferases, Histone Acetyltransferases (HATs) and by affecting biochemical pathways. The 'indirect epigenetic pathway' exerts its effects by affecting the signaling pathways [13,21]. YBLI also aids by correcting any aberrations in the imprinting centers and thus maintaining a balance in the activity of maternally and paternally imprinted genes [22]. YBLI thus restores genomic stability by regulating levels of OS and maintain mitochondrial and genomic integrity and telomere length [11,13,19].

There is a secular trend of decline in male reproductive health. This is seen by a decline in semen quality, increased incidence of genitor urinary abnormalities and increased incidence of gonadal tumors in the reproductive age group. This rapid decline is due to unhealthy social habits, lifestyle and exposure to environmental pollutants. Adoption of YBLI have aided in the rescue of such problems as shown in previous studies conducted in our laboratory. Various complementary and alternative medicine techniques have been proved to be not only effective in maintaining but also in regulating and enhancing reproductive health in men to produce a successful pregnancy outcome. Yoga practice has beneficiary effects for both male and female partners by minimizing stress, consecutively balancing the hormonal status of the body, with improvement in mental health and quality of life; further increasing the couple's ability to conceive, increase the carry home birth rate. Regular yoga practice from childhood until seeking fertility is beneficial for reproductive health by reversing or preventing adverse epigenetic modifications and enabling healthy epigenetic imprints and avoiding adverse transgenerational effects. This calls for an in depth research in this virgin field of therapeutic effects of yoga to achieve complete health and further investigation into this relationship using large, well-defined populations, adequate controls, randomization and long duration should be explored. Thus yoga is recommended in idiopathic cases of early pregnancy loss to not only improve reproductive health and outcome but to overall improve quality of life.

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