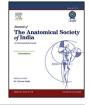
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# Original Article Impact of mindfulness based stress reduction on sperm DNA damage



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## ABSTRACT

*Introduction:* Sperm DNA damage is the major cause of defective sperm function. Poor social habits take a toll not only on reproductive health of parents but the resultant offspring too. Adopting a holistic integrated approach like mindfulness based stress reduction (MBSR), a yoga based intervention have gained significant impetus in recent years. This study aimed to analyze how mere a simple lifestyle change can bring about balance in seminal oxidative stress parameters and related consequences in next generations.

*Methods:* Out of 126 fathers of children with non-familial sporadic heritable Retinoblastoma (NFSHRb), 102 were randomized into 2 groups i.e. MBSR group and Non-MBSR group. Parameters of seminal oxidative stress (OS) and oxidative DNA damage (ODD) were measured at baseline (0 day) and after 4 weeks in both groups. *Results:* There was significant decrease (p < 0.0001) in mean reactive oxygen species (ROS), DNA fragmentation index (DFI) and 8-hydroxy-2'-deoxyguanosine (80HdG), increase (p < 0.0001) in mean total antioxidant capacity (TAC) post 4 weeks of MBSR whereas non-intervention group showed opposite trends when compared with baseline.

*Discussion:* A 4-week MBSR resulted in significant improvement in sperm DNA integrity and regulation of OS may affect the sperm epigenome, reduces *de novo* germline mutation rate and affects lifelong health trajectory of offspring. In the era of limited space, commercial expansion and increased incidence of complex lifestyle diseases, there is a dire need to adopt an integrated system of mind body interventions which aims to achieve physical, mental, spiritual wellbeing and improve quality of life.

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## 1. Introduction

Sperm DNA damage is the common underlying etiology of idiopathic infertility, recurrent spontaneous abortion, recurrent implantation failure and congenital malformation.<sup>1,2</sup> Oxidative stress (OS) is the chief cause of DNA damage and can occur due to a host of exogenous and endogenous factors, majority of which are modifiable.<sup>1,3</sup> Unhealthy lifestyle like intake of fast foods (nutritionally depleted processed food), sedentary lifestyle, smoking, alcohol consumption, psychological stress, depression can result in overproduction of reactive oxygen species (ROS) exceeding the body's natural antioxidant defenses resulting DNA damage. Mitochondrial damage precedes nuclear DNA damage and is more severe. Sperm works in concert with the oocyte to repair the damaged DNA as it has the only enzyme in the base excision repair (BER) pathway, 8-oxoguanine glycosylase 1 (OGG1) and lacks downstream DNA repair genes like *APE* and *XRCC1*. As sperm

\* Corresponding author. E-mail address: rima\_dada@rediffmail.com (R. Dada). has a limited capacity for detection of DNA damage and repair, sperm DNA damage if extensive, may persist post fertilization and lead to accumulation of damaged DNA in each cell of zygote. This occurs due to aging oocyte with aberrant and incomplete DNA repair and hence the accumulation of oxidized DNA adducts. Some of these adducts like 8-hydroxy-2'-deoxyguanosine (80HdG) are mutagenic and also induce epimutations. Presence of bulky 80HdG adduct in proximity to the cytosine base at CpG islands in promoter regions prevents methylation and induce genome wide hypomethylation and genomic instability. 80HdG also results in 18 fold higher mutation rate and 200 fold increase in GC>TA transversions. This predisposes to both *de novo* germline mutations in fathers and somatic mutations in the offspring.

With the addition of mutagenic oxidative adducts, there may be accumulation of mutations in both sperm DNA (germline) or in zygote (somatic), which may increase risk of development of several autosomal dominant disorders, complex neuropsychiatric disorders and even pediatric cancer (leukemia, neuroblastoma, lymphoma, osteosarcoma, retinoblastoma, rhabdomyosarcoma).<sup>4</sup> Many studies have reported a negative impact of poor lifestyle factors on testicular function, spermatozoa parameters and

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Nomenclature			
Abbrevia	ations		
NFSHRb	Non-familial sporadic heritable retinoblastoma		
DFI	DNA fragmentation index		
ROS	Reactive oxygen species		
MBSR	Mindfulness based stress reduction		
OS	Oxidative stress		
ODD	Oxidative DNA damage		
80HdG	8-hydroxy-2'-deoxyguanosine		
TAC	Total antioxidant capacity		
Units			
ROS	Relative Light Unit (RLU)/sec/million sperm		
DFI	%		
80HdG	pg/ml		
TAC	mmol/Trolox equiv/L		

pituitary-gonadal axis dysfunction.<sup>5,6</sup> For the reversal of OS, there are several antioxidants available which may increase sperm concentration and motility, but only few of them affect sperm DNA integrity and thus results in transmission of damaged DNA to the offspring.<sup>7</sup> Long-term indiscriminate usage of anti-oxidants may disrupt the homeostatic redox balance and can lead to "Reductive Stress" and result in premature DNA decondensation.<sup>3</sup> Till date no single intervention is able to modulate and regulate the redox homeostasis avoiding free radical induced oxidative injury.

Yoga and meditation is an emerging health discipline as a complementary integrative alternative therapy which aims to promote health and prevent disease. In the age of super specialization, this is the alternative holistic modality which targets the mind and body as a whole. All diseases have psychosomatic component and thus there is a need to adopt a holistic approach in management of diseases. Yoga is a technique of well-being and consists of asanas, pranayama and dhyana. Various studies on Yoga intervention have highlighted a positive change in the deranged biomarkers of disease and health like glycemic outcomes<sup>8</sup> & lipid profiles,<sup>9</sup> BMI & blood pressure,<sup>10</sup> inflammatory markers<sup>11</sup> and depression scales.<sup>12</sup>,<sup>13</sup>

A recent study from our lab demonstrated improvement in biomarkers of cellular aging and longevity in apparently healthy population after voga based lifestyle intervention.<sup>14</sup> After the successive positive preliminary results, this study aims to analyze the actual role of simple lifestyle interventions like voga and meditation in balancing the seminal redox homeostasis.<sup>15,16</sup> Yoga targets both mind and body via a well-defined psychoneuroendocrine pathway and improves cardio-vagal tone which further affects a wide array of downstream processes ranging from basic metabolism, organ system maintenance, epigenetics, DNA repair, oxidative bioprocesses to aging, blood pressure, subjective wellbeing, and reproductive health. Biochemical and microarray studies on impact of yoga on primary open angle glaucoma (POAG), depression, infertility have shown a significant increase in expression levels of genes regulating DNA repair, anti-inflammation, cell cycle regulation and reduced expression of proinflammatory genes.<sup>12,13,17</sup> Therefore, the main aim of the present study was to evaluate impact of MBSR on seminal oxidative stress and oxidative damage in sperm DNA in fathers of children with nonfamilial sporadic heritable Retinoblastoma (NFSHRb).

# 2. Material & methods

# 2.1. Study design and participants

A total of 126 fathers of children with NFSHRb reporting at Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi were enrolled but 6 fathers declined to participate and 8 of them harbored somatic mutations in *RB1* gene. Randomization was done into two groups i.e. mindfulness based stress reduction (MBSR) group and Control intervention (non MBSR) group (Fig. 1). Ethics Committee Approval was obtained with the reference no: IESC/T-364. After obtaining

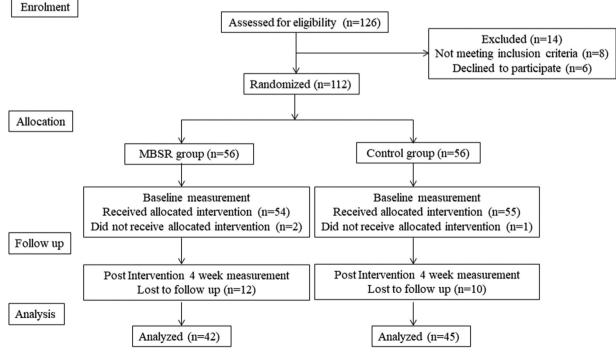


Fig. 1. Flow diagram of enrolment and follow up.

written informed consent, the fathers underwent a baseline assessment. A structured questionnaire was used to obtain information on demographic characteristics, birth-related factors, childhood medications, residential history and familial and genetic factors, as well as on maternal and paternal medications, occupation and other environmental and lifestyle factors. Fathers were asked about their smoking habit, tobacco consumption and alcohol use, specifically the number of cigarettes usually smoked per day, tobacco usage and alcohol consumption over the last 10 years before providing the sample. Fathers who were taking any kind of anti-oxidants or corticosteroids during or 3 months prior to the study period were

excluded. Semen samples were obtained from all the fathers at day 0 (baseline) followed by subsequent measurements at 4th week after the intervention.

### 2.2. Intervention

#### 2.2.1. Mindfulness based stress reduction (MBSR) program

The design of 4 weeks pretested MBSR program, a yoga based intervention was published previously in detail by our laboratory.<sup>14</sup> Instructor driven yoga sessions were conducted for 120 min on 5 days per week during 4 weeks. Even after the completion of 4 weeks program under the supervision of instructor, the patients were regularly followed up to 6 months. The patients have been provided with the pamphlets depicting yogic postures and a video recording of complete session to be done by them at home. The compliance of the home based MBSR program was monitored through maintenance of a daily log and a regular telephonic contact.

#### 2.2.2. Intervention for Non-MBSR control group

Participants of this group were advised to follow their normal day to day physical activities without any change in their lifestyle in terms of physical activity like running, walking or any other aerobic exercises. They were advised to continue their normal routine lifestyle.

#### 2.3. Outcome measures

The study outcomes were markers of OS i.e. ROS and TAC and markers of ODD i.e. 8OHdG and DNA fragmentation Index (DFI). Along with the experimental parameters, anthropometric measurements like weight and height were also recorded by standard methods at the beginning before randomization and at the end of 4 weeks at a post MBSR program visit. The following protocols were used for the estimation of the study outcomes.

#### 2.3.1. Semen analysis

Semen analysis was performed as per the guidelines of the WHO 2010.  $^{\rm 18}$ 

#### 2.3.2. Chemiluminescence assay

ROS detection was performed by chemiluminescence assay in neat semen according to protocol described earlier.<sup>19</sup>

#### 2.3.3. Sperm chromatin structure assay (SCSA)

The SCSA was performed according to the procedure described previously.<sup>20</sup>

#### 2.3.4. Enzyme-linked immunosorbent assay (ELISA)

ELISA was performed for the estimation of total 80HdG and total anti-oxidant capacity (TAC) in sperm DNA and seminal plasma samples respectively. 80HdG and TAC levels were made using ELISA (Cayman Chemical, USA) following manufacturer's protocol.

#### 2.4. Statistical analysis

Mean and Standard Deviation were computed for all the measurable study variables for each intervention group. To test significance of the differences in mean values of the study variables, from basal to the follow-up period within each group, paired *t*-test was applied whereas for between the group analyses, unpaired *t*-test was applied. The mean change scores of outcome variables were analyzed using paired-samples *t*-test. The p value less than 0.05 was considered as statistically significant. Effect size of the study outcomes were calculated for the analysis of clinical significance, magnitude and direction of MBSR program's effect with respect to the control intervention. The same was calculated for each outcome via the formula for Cohen's d,<sup>21</sup> along with 95% confidence intervals.

# 3. Results

One twenty six fathers (cases) of children with NFSHRb with no family history of Retinoblastoma and 14 fathers were excluded due to various reasons (Fig. 1). Thus, 112 fathers were randomized into two groups. The baseline measurements were taken at day 0 for all experimental parameters and their demographic characteristics were also noted. Out of 56 fathers, 54 received MBSR program and 12 lost to follow up at 4th week, hence 42 fathers were analyzed. Similarly, in control group 55 fathers received intervention and 10 lost to follow up, hence 45 fathers were analyzed. The sociodemographic characteristics, social habits and semen analysis of the population at baseline showed no significant differences between the two groups indicating that they are comparable (Table 1).

On the basis of detailed history of social habits of the fathers, 4 groups were made i.e. smokers, non-smokers, alcohol consumers and alcohol non-consumers. By definition, non-smokers had never smoked or consumed any variant of tobacco, whereas all smokers had smoked cigarettes for at least 1 pack years (a pack year is defined as 5 cigarettes per day for 4 years) before the conception of the index subject (henceforth referred to as preconception smoking) and after the birth of the index child. Fathers who were current or former cigarette smokers were asked detailed information about the number of cigarettes smoked per day and the cumulative duration of smoking before the conception of the index subject and after the birth of the index child, respectively. By definition, Alcohol consumers were the ones who had more than 5 drinks per day on an average (1 or more alcohol binges per month) whereas alcohol non-consumers had never consumed alcohol in any beverage. Fig. 2 shows the distribution of subjects on the basis of their social habits in both the groups.

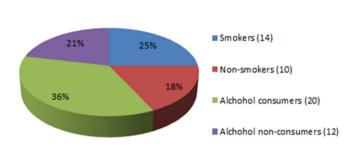
After 4 weeks of MBSR program there was significant improvement seen in the OS and ODD parameters like ROS, DFI,

#### Table 1

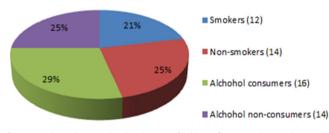
Comparison of baseline values in MBSR group and Control group.

Variable	MBSR Group (n=56)		Control Group (n=56)		
	Mean	SD	Mean	SD	
Demographic Characteristics					
Age of fathers	33.8	7.16	32.9	5.02	
Age of children	1.6	0.4	1.41	0.75	
BMI (kg/m <sup>2</sup> )	23.1	2.36	23.5	3.61	
Semen Analysis Measurements					
рН	7.81	0.25	7.78	0.43	
Volume (ml)	3.25	1.6	3.9	0.80	
Liquefaction time (min)	32.5	4.4	30.5	4.75	
Progressive motility (A+B)	52.65	16.56	55.85	13.15	
Sperm Count (million/ml)	112.05	17.6	115.51	44.8	

# YMLI Group



# **Control Group**

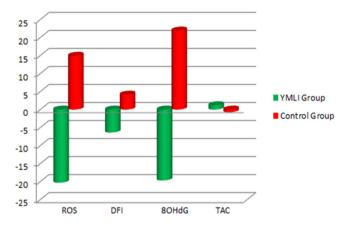


**Fig. 2.** Pie-chart showing the distribution of subject of MBSR and Control group into four categories according to their lifestyle habits.

TAC and 8OHdG when compared to their baseline values (Table 2). MBSR has brought significant differences in the experimental parameters over a period of 4 weeks (Fig. 3). A differential fall of mean ROS was 20.29 [CI (-29.10, -11.48)] RLU/sec/million sperm with MBSR and an increase of 14.93 [CI (10.40, 19.47)] RLU/sec/million sperm in control group. There was a significant decline in

#### Table 2

Analysis of outcome measures in study completers.



**Fig. 3.** Mean change scores of study parameters in MBSR and Control group over a period of 4 weeks from baseline (0 Day).

the mean DFI percentage of 6.36 [CI (10.40, 19.47)] % in MBSR group whereas the mean DFI percentage increased in control group with 4.15 [CI (3.132, 5.170)] %. Sperm DNA fragmentation i.e. DFI as measured by SCSA measures the susceptibility of sperm DNA to acid-induced DNA denaturation *in situ* indicated the fraction of defective spermatozoa showing the presence of DNA breaks (only two subjects shown) and pattern of decrease in % DFI post 4 weeks of MBSR and %DFI increase in control group after 4 weeks. A mean fall of 19.66 [CI (-26.59, -12.74)] pg/ml in 80HdG levels was seen in MBSR group whereas 21.93 [CI (16.82, 27.03)] pg/ml increase was seen in control group over 4 weeks' time. TAC levels in MBSR group increased significantly by 1.21 [CI (0.77, 1.64)] mmol/Trolox equiv/L compared to a decrease of 0.72 [CI (-0.98, -0.46)] mmol/Trolox equiv/L in control group.

The effect size of MBSR program relative to control group was estimated for each outcome measure using change mean score data from the fathers who completed the assigned interventions (n = 87) (Table 3). The Cohen's d effect size of MBSR program was relatively large in reducing ROS, DFI and 80HdG levels at -1.5 [95%

Intervention Group	Outcome Measure	Baseline measurement Mean (SD)	Post 4 week measurement Mean (SD)	p-value Within the groups	Change from Baseline to 4 week Mean (SD) [95% CI]	p-value Between the groups
MBSR Group	ROS (RLU/sec/million sperm)	51.73 (6.65)	31.45 (4.55)	<0.0001	-20.29 (28.27)	<0.0001
(n=42)	(RE0/See/minor Sperm)	(0.05)	(1.55)		[-29.10, -11.48]	
Control Group		52.36	67.30	<0.0001	14.93	
(n=45)		(2.76)	(3.13)		(15.10) [10.40, 19.47]	
MBSR	DFI	29.99	23.62	<0.0001	-6.36	< 0.0001
Group (n=42)	(%)	(0.89)	(1.3)		(9.25) [-9.252, -3.487]	
Control Group		28.80	32.95	< 0.0001	4.15	
(n=45)		(0.85)	(0.92)		(3.39) [3.132, 5.170]	
MBSR	80HdG	99.50	79.84	<0.0001	-19.66	< 0.0001
Group (n = 42)	(pg/ml)	(3.41)	(3.00)		(22.23) [-26.59, -12.74]	
Control Group		96.74	118.7	<0.0001	21.93	
(n=45)		(2.69)	(3.41)		(17.00) [16.82, 27.03]	
MBSR	TAC	3.557	4.762	<0.0001	1.21	< 0.0001
Group $(n=42)$	(mmol/Trolox equiv/L)	(0.22)	(0.23)		(1.40) [0.77, 1.64]	
Control Group		3.738	3.016	<0.0001	-0.72	
(n=45)		(0.19)	(0.16)		(0.85) [-0.98, -0.46]	

Table J							
Effect sizes	for	outcomes	measures	in	study	completers.	

Outcome	Mean Change Score (SD)	Between-group Effect Size		
Measure	MBSR Group (n=42)	Control Group (n=45)	(Cohen's d <sup>*</sup> ) with 95% Cl	
ROS (RLU/sec/million sperm)	-20.29 (28.27)	14.93 (15.10)	-1.5 (-2.1, -1.1)	
DFI (%)	-6.36 (9.25)	4.15 (3.39)	-1.5 (-2.0, -1.1)	
80HdG (pg/ml)	-19.66 (22.23)	21.93 (17.00)	-2.1 (-2.6, -1.5)	
TAC (mmol/Trolox equiv/L)	1.21 (1.40)	-0.72 (0.85)	1.6 (1.2, 2.1)	

Cl, -2.1 to -1.1], -1.5 [95% Cl, -2.0 to -1.1] and -2.1 [95% Cl, -2.6 to -1.5] respectively whereas in increasing TAC levels at 1.6 [95% Cl, 1.2-2.1]. The negative values in the confidence interval indicated the direction of effect, at least 95% of the time, would be towards reducing ROS, DFI and 80HdG levels. The positive values in the confidence interval indicated the direction of effect of MBSR, at least 95% of the time, would be towards increasing TAC levels. All values in the effect size were noted to rise above an absolute value of 0.80, the upper threshold proposed by Cohen to represent a large and appreciable clinical effect. Yoga appeared to exert a large, positive clinical effect in increasing TAC values and decreasing ROS, DFI and 80HdG values.

# 4. Discussion

ODD and accumulation of 80HdG predisposes to de novo germline mutations in sperm DNA and somatic mutations in offspring. Accumulation of this base also impairs methylation at CpG islands in promoters of genes and thus increases the incidence of genetic and epigenetic diseases in the offspring. The findings from this RCT indicate that smoking and alcohol consumption by father impacts the semen quality over the passage of time whereas lifestyle modifications like yoga can significantly reduce OS and ODD. Sperm is most vulnerable to environmental insults as it has minimal cytosolic antioxidants and a highly truncated DNA repair mechanism. Sperm epigenome is also highly sensitive to the changes in environment, social habits and lifestyle. The effect of these factors is dependent on dose and duration of the exposure.<sup>1,4,15</sup> This study mainly focusses on the poor lifestyle/ social habits adopted by fathers of children with NFSHRb especially smoking and alcohol consumption. Thus it is important to increase awareness that the germ cells have a memory and accumulate various changes right from the time the parents themselves are conceived. Thus good habits need to be an integral part of our lifestyle rather than just be adopted 3-4 months prior to planning a child as biological parenting begins much before conception, when parents themselves are conceived. Smoking leads to increase in levels of ROS and ODD, decrease in mitochondrial activity, leukocytospermia, telomere shortening and increase in incidence of childhood cancer.<sup>15</sup> The inflammatory response induced by smoking leads to activation of seminal leukocytes and increased ROS production.<sup>22</sup> The risk of occurrence of retinoblastoma in the children of fathers who smoke was 4 times higher than the cases who did not smoke i.e. OR 4, 95% CI: (0.7-23.1), and but was not significant (p=0.155). Excessive alcohol consumption causes an increase in systemic OS as ethanol stimulates the production of ROS, and the odds of occurrence of retinoblastoma in children of alchohol users was 13.3 times greater i.e. OR 13.3, 95% CI: (1.1-166.4), and was statistically significant  $(p=0.044^*)$ .<sup>4</sup> During alcohol metabolism, carcinogens like acetaldehyde are generated, which interfere with DNA replication; impair the process of DNA repair and form DNA adducts which trigger replication errors and/ or mutations in oncogenes and in tumor suppressor genes. Thus unhealthy social habits and poor lifestyle factors trigger OS which lead to disruption of sperm function by peroxidative damage to the sperm plasma membrane, cause carbonylation of proteins, DNA fragmentation in sperm nuclear/mitochondrial genome and dysregulation in levels of sperm transcripts.<sup>4,14,23</sup> In a study from our laboratory, we also observed that seminal 80HdG levels in fathers of sporadic Retinoblastoma patients was higher as compared to fathers of healthy children i.e. 80HdG [117.4 (72.2,162.1); 78.2(33.6,127.6); p < 0.0001]. Similarly, the values of blood plasma 80HdG levels were higher amongst Retinoblastoma children (n = 126) as compared to healthy children (n = 126) i.e. 80HdG [902(224.9,5195.7); 478.1(113.3, 988.1); p < 0.0001].<sup>24</sup>

In the current study, MBSR group showed the significant reduction in OS (within 10 days) and reduction in ODD over a period of 4 weeks (significant improvement in 6 months). A recent review on mind body interventions has documented improvement in expression of genes related to energy metabolism, mitochondrial function, improved COX-2 activity, insulin secretion, and telomere maintenance and normalized expression of genes involved in inflammatory reactions and stress pathway thereby improving mental and physical health.<sup>25</sup> Tolahunase M et al reported an improvement in mitochondrial integrity, decline in ROS levels and lower expression of inflammatory cytokines following YMLI.<sup>14</sup> There was an increase in levels of serotonin, melatonin and BDNF in individuals who practiced YMLI and thus reduced stress and anxiety scores and improved overall quality of life.<sup>12,13,14</sup> A recent study from our lab documented that YMLI also upregulates the expression of antioxidant, anti-inflammatory genes and that of telomerase enzymes, which both aid in maintenance of telomere length and genomic stability.<sup>12,13,15</sup> In majority of cases of NFSHRb, it's the last born child which is affected as the father's age is usually greater than 35 years. Advanced paternal age is associated with mitochondrial DNA damage, increased free radical levels and decreased ATP production. Endogenous antioxidants such as superoxide dismutase, catalase, pyruvate and ascorbic acid etc. in seminal plasma scavenge ROS and protect spermatozoa from oxidative stress. Thus, antioxidants reduce cellular levels of ROS by inactivating the ROS produced by various metabolic activities and by decreasing the level of enzymatic ROS production. Overuse of antioxidants may lead to reductive stress however the impact of anti- oxidants on DNA is still marked by controversy and very high dosage of antioxidants results in premature DNA decondensation and can impair pronucleus formation. It can disrupt the intricate oxidationreduction balance, can lead to reductive stress, thus the indiscriminate usage of anti-oxidants should be avoided and rather healthy lifestyle should be adopted like MBSR which aims at regulation of optimal ROS levels rather than simply lowering them.<sup>12,14</sup> In this study, the mean change levels of TAC post 4 weeks of MBSR were found to be positive i.e. 1.21[95% CI, (0.77-1.64)] mmol/Trolox equiv/L. This effect can be attributed to the activation of cardio vagal tone (parasympathetic nervoussystem), optimizing secretion of sympathetic hormones such as cortisol and catecholamine (regulation of hypothalamo-pituitary adrenal axis) and elevation in levels of antioxidants such as melatonin.<sup>26</sup> Quitting smoking, avoiding excessive exposure to pesticides, insecticides or herbicides, reducing excessive alcohol intake, avoid intake of nonvegetarian food items (high levels of xenoestrogens, antiandrogenic chemicals in animal meat), environmental toxicants, minimizing psychological stress, increasing intake of food items rich in dietary antioxidants, vitamins and whole plant based nutrient dense diet can prevent OS and delay onset of complex lifestyle diseases and delay the rate of aging.<sup>3</sup>

Our study documented that 4 weeks of MBSR exerts large effect size hence can become an adjunct therapy to counter psychological and seminal oxidative stress and thus lower the burden of complex disorders. Yoga attenuates the stress cascade via downregulating the HPA axis which gets hyperactivated as a response to any external or internal stressor and yoga improves cardio-vagal tone.<sup>12,27</sup> It also reduces psychological stress, anxiety and depression. A study from our laboratory showed that YMLI causes upregulation in levels of neurotrophins like BDNF, DHEA (a pleiotropic steroid), melatonin and serotonin.<sup>14</sup> Yoga is a science and a technology of well-being which is a mind body technique and improves overall health and is the need of the hour in this age of super specialization. Melatonin not only regulates the circadian rhythm but is a master regulatory molecule with antioxidant and oncostatic activities. Serotonin improves well-being and can minimize usage of antidepressants. As majority of diseases have a psychosomatic component, a holistic approach is ideal in promoting health and should be used as an adjunct to medical therapy. Yoga therapy is thus cost effective, noninvasive, has minimal risk of adverse/side effects or drug interactions.<sup>28</sup> It also normalizes the levels of sperm transcripts such as FOXG1, WNT5A, SOX3, and STAT4 which play a critical role in embryogenesis and can reduce incidence of idiopathic early pregnancy losses.<sup>13,16</sup> Thus as MBSR reduces both OS and ODD. thus may reduce incidence of genetic and epigenetic diseases. Cancer is a disease of the genome and MBSR program including yoga can improve both mitochondrial and nuclear DNA integrity and reduce the incidence of de novo germline mutations in sperm and affect health trajectory of the offspring.

#### 5. Conclusion

MBSR can regulate levels of OS and ODD damage by maintaining a molecular homeostasis of redox reactions, improvement of sperm mitochondrial and DNA integrity and regulation of sperm transcripts. It can thereby reduce the incidence of sporadic childhood cancers. This reduction in incidence occurs due to reduction in the levels of mutagenic bases (80HdG) which can induce both genetic mutations and epimutations. Simple modification in lifestyle and adoption of MBSR technique like yoga can significantly positively impact the paternal mitochondrial and nuclear genome integrity thereby improving health of offspring.

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