REVIEW OF LITERATURE

The rationale and the basis of the present study is that professional sports activities could induce a genetic damage response probably from the oxidative stress generated as a result of excessive oxygen uptake during strenuous training and sports activities. Furthermore, genetic damage could be modulated by those metabolic and antioxidant genotypes capable of scavenging and for balancing the free radicals. The framework of this chapter therefore includes background information on various aspects of sports and related activities as well as details about the games of the study participants and the induction of oxidative stress from strenuous exercise and the literature on exercise-induced oxidative stress and exercise-induced genetic damage have been reviewed. The review on lipidemia in sports persons, association of genetic variants with sports performance, and with genetic damage along with details of the gene polymorphisms studied in the present work with studies documenting association with increased/decreased oxidative stress and/or genetic damage in patients and in persons in different occupations as well as in sports, has also been covered.

2.1 Background on Sports-related Aspects

Sports and games are an integral component in the all-round development of the human personality. Besides being recreational and a source of entertainment, they have found prominence in physical fitness programmes. Professional sports also foster physical fitness and sports have played a great role in the generation of the spirit of healthy competition and bonding within the community as well as in international relationships (Yacht, 2012-2013).

2.1.1 Importance of Sports

Sports have been considered as an integral part for overall development of an individual’s personality. The activity helps in developing leadership qualities, team spirit, self-confidence, discipline, decisive-attitude, health fitness and popularization of sports encourages business market therefore providing employment to many. Sports activities help in the development of social skills like interaction and communication

2.1.2 Sports in India

In ancient India, the Vedic era has mention of games of strength and speed and physical activity. Some games having Indian origin include chess, wrestling, polo and archery (facts-about-india.com, accessed on April 6, 2014) associated with religious rights. Presently, the development of sports is under the purview of the Ministry of Youth Affairs and Sports and the National Sport Federations (GoI, accessed on April 6, 2014) and they are also responsible for the promotion of sports. The Sports Authority of India (SAI) supports and nurtures talent in the youth, besides providing the infrastructure, equipment, coaching facilities and competition exposure (Sports authority of India, accessed on April 10, 2014).

2.1.2.1 Sports in Punjab- The state of Punjab (50,362km) in the north-western part of the country extend from the latitudes of 29.30° North to 32.32° North and longitudes of 73.55° East to 76.50° East (Environment Statistics of Punjab, 2011). The state has a pre-eminent position in the realm of sports having furthered under the guidance of the Department of Sports, Punjab, since 1975. Punjab is the only state with most astro-turf hockey fields, synthetic tracks and ultra-modern sports infrastructure (Department of Sports, Punjab accessed on April 10, 2014). Sports goods industry has become a major cottage industry with about 10,000 workers with Jalandhar as the nucleus of the industry in Punjab having ~90% of the country’s total sports good units (Sports Good Industry, Jalandhar; accessed on April 7, 2013).

Punjab has a very rich background in sports and Duggal (2010) has traced that sports in Punjab emerged as a means of entertainment, and becoming a lifelong profession for some. Rural sports in Punjab however started as a part of the day-to-day activities in order to provide defense from common enemies and animals and for developing physical strength required for farming (Rural Sports in Punjab, accessed on April 10, 2014). Sports tournaments had been a regular feature in older days with sports competitions at village levels and the organization of different sports at Anandpur Sahib
doing *Holla Mohalla* celebrations from the time of the *Sri Guru Gobind Sahib ji* (Discover India). These have since developed as annual sports events in the ~7000 villages of Punjab and include acrobatic displays, gymnastics, riding, fencing, archery, tent-pegging, wrestling and kabbadi.

Modern sports are finding popularity and many Punjabis are bringing accolades to the state hockey, cricket, wrestling, shooting, athletics and golf (Duggal, 2010). Paralympics as well as Indo-Pak games are other events being regularly held here and there foster brotherhood and sportsmanship.

### 2.1.2.2 Sports in Amritsar-

The city of Amritsar (31.63°N, 74.87°E) situated in northern Punjab state of northwestern India lies about 15 miles (25 km) east of the border with Pakistan. Amritsar meaning ‘the pool of Nector’, most holy place of Sikhs, is an important city in Punjab and is a major commercial, cultural and transportation center. It is also the center of Sikhism and the site of the Sikh’s principal place of worship. Sports has an ancient history in Amritsar as the Sikh ‘Nihangs’ (warriors) were required to keep themselves mentally as well as physically fit and thus was born the tradition of sports and calisthenics in this holy city (Maps of India.com, accessed on Feb 7, 2014).

Among earliest mentions of sports is that of wrestling bouts held within the premises of the *Akal Takht Sahib* endorsed by Sri Guru Hargobind Sahib ji for toughening the body frames, and strengthening the minds of the Sikhs (Kilalampur Sports Festival). The city’s Gandhi Sports Complex ground, a multi-faceted sports facility with accommodation facilities for sports persons, is well-equipped with sports equipment and facilities for hosting intra-state and national tournaments.

Guru Nanak Dev University, Amritsar is leading in sports having won the coveted Maulana Abdul Kalam Azad Trophy 21 times in succession (Department of Physical Education, Guru Nanak Dev University, accessed on March 27, 2014). The trophy is awarded by the Government of India to a university for excellence in sports performance. The other local institutes in the city also provide spacious playgrounds and facilities to promote sports.
Recently, the Punjab government has initiated plans to develop Amritsar as the state’s sports-hub by creating facilities to host sports events and provide world class sports-infrastructure for budding players. Also an international state-of-the-art stadium-cum-sports complex is on the anvil (Rana, 2013).

2.1.3 Classification of Sports

Classification of sports has been done on the basis of different aspects depending on the types and intensity of exercises required for various sports (Mitchell et al., 2005), being team or individual sports, on the basis of bioenergetics characteristics, or sports training (Boraita, 2004)

2.1.3.1 Types and Intensity of Exercises– Depending on the specific game requirement, the types and intensity of exercises performed are different. Mitchell et al. (2005) have classified sports type as IA, IIB and IIIC based on their dynamic and static demands. The type IA exercises have low-static and low-dynamic demand; IIB has moderate-static and moderate-dynamic while IIIC demands high-static and high-dynamic exercises. Dynamic exercises, also known as isotonic exercises, are for strength-training and include running, playing soccer or squash and swimming. Strength-training involves changes in muscle movement with increased oxygen consumption.

2.1.3.2 Team and Individual Sports- Hockey, handball, softball playing as well as athletics require both aerobic as well as anaerobic system of the body. Among these, athletics requires more endurance since it is a short time sport, where the target has to be reached in a short time span and has to be individually achieved while other sports are team sports and have varying time periods for which the game matches are held.

2.1.3.3 Classified Depending on the Bioenergetic Characteristics (Boraita, 2004)- These can be aerobic or anaerobic.

Aerobic- In this type, long-duration, and light-moderate intensity exercise dominates, in which the oxygen supply is essential for obtaining energy. These include the marathon, long distance swimming, tour cycling.
Alactic anaerobic- In this there is short, high intensity exercise in which energy is provided by ATP and phosphocreatine and it includes 50 m and 60 m track events.

Lactic anaerobic- This is short duration and high intensity exercise like the 400 m track events.

Mixed- This includes aerobic/anaerobic exercises and soccer, basketball, volleyball etc. are of this type.

2.1.3.4 Classified Depending on the Methodology of Sports Training (Boraita, 2004)- Sports are also classified as being strength and explosive strength sports (weightlifting, jumping, throwing), combat sports (boxing, fencing, judo), endurance sports (medium and long distance track events, swimming for >100m events, tour cycling), ball sports (soccer, volleyball, basketball), and coordination and competitive art sports (gymnastics, synchronized swimming, etc).

2.1.4 Sports/Games of the Present Study Sports’ Participants

The sports groups had equal representation of handball, hockey, baseball-softball and athletics. The first three are intermittent, team ball-sports while athletics is endurance type and individual sport. All these are generally IIB sports categories with moderate-static and moderate-dynamic required exercises (Mitchell et al., 2005). For these sports, the players optimally (Mitchell et al., 2005) should have 40-70% of maximum oxygen uptake (VO$_{2\max}$); the VO$_{2\max}$ is the amount of oxygen breathed in one minute while working at full capacity. It’s a measure of fitness expressed in milliliters per kilogram per minute (Vema et al., 2009).

2.1.4.1 Handball- Handball is also an intermittent team sport (Zapartidis et al., 2009) and is categorized as a high dynamic, low-static sport (Mitchell et al., 2005). The sport requires training for throwing, flexibility and optimal velocity with VO$_{2\max}$ of 46-55ml/kg/min in females and 55-60ml/kg/min in males (Zapardatis et al., 2009) which have been categorized as having superior to good aerobic capacity (Heywood et al., 2006). In India, it is a popular sport played at the local level though the first national team was formed in 1989. The Handball Federation of India manages the game in India (Handball India, accessed on April 15, 2014).
2.1.4.2 Hockey - Among the top six sports in the world, the origin of Hockey is ancient. The British introduced the game in India in 1885 and presently the Indian Hockey Federation promotes the sport (Sport Field Hockey, accessed on March 6, 2014). Hockey was originally played on grass surfaces which continued until the introduction of artificial turf in 1970s, bringing some changes in the game. It is an intermittent team sport requiring high-dynamic, low-static exercises involving short sprinting and movements, with and without the ball (Mitchell et al., 2005).

2.1.4.3 Baseball and Softball - These are both moderate-dynamic, moderate/ low-static intermittent sports (Mitchell et al., 2005). They require similar training and the exercises for these sports include shoulder exercises, throwing, pitching and arm-strengthening and VO\(_{2}\)\(_{\text{max}}\) of 48-56ml/kg/min in females and 52-57ml/kg/min in males (Wilmore and Costil, 2005). These games were introduced to India in 1983 (Baseball) and 1961 (Softball) and Amateur Baseball Federation of India (http://www.baseballindia.com/ accessed on 24 March, 2014) and Softball Association of India (Softball Association of India, accessed on accessed on 24 March, 2014) manages their development and promotion. Baseball is preferred by males while females prefer softball, the latter more popular at school and at the university levels.

2.1.4.4 Athletics - Athletics comprises sporting events such as competitive running, jumping, throwing and walking as taking part in track and field events, road running, cross country running and race walking. Not requiring sophisticated equipment, athletics is a most competed sport. It is an individual sport but relay and cross-country running requires teams. Athletics is an endurance sport requiring muscle power strengthening, body combination/ coordination (Willmore and Costill, 2005). It is high-dynamic, low-static sports category (Mitchell et al., 2005) and a VO\(_{2}\)\(_{\text{max}}\) of 60-85ml/kg/min in males and 50-75ml/kg/min in females (Willmore and Costill, 2005). The Athletics Federation of India started in India in 1946 and continues to promote athletics in the country.

2.1.5 Sports as a Profession

In India, professional sports is not considered because of lack of career options except in the field of cricket. In other countries like china, Japan, Kenya and South Korea,
sports professions are opted for since the government supports with the basic infrastructure and facilities. This is the reason that though India is the second populous country in the world, yet the medal-tally in Olympics is low.

2.2 Oxidant Stress vis-à-vis Strenuous Exercise

Regular exercise and moderate physical or sports activity have the potential for health benefits and afford protection against various causes of mortality by reducing risks of developing cardiovascular diseases and diabetes, and delay the ageing process (Cicek, 2006; Reichhold et al., 2009). However, acute and strenuous exercise does not elicit the same response as there is increased demand for oxygen uptake/consumption, which can be up to 10-15 fold (Shi et al., 2007; Andersson et al., 2009). Such an oxygen uptake can disturb the intracellular pro-oxidant-antioxidant homeostasis and increase the free radical production (Ji, 1999). Free radicals are active due to the presence of single, unpaired electrons in chain reactions. These are produced through different physiological reactions (Marciniak et al., 2009) and include reactive oxygen species (ROS) and reactive nitrogen species (RNS). Exercise-induced free radical formation occurs from increased mitochondrial oxygen consumption needed during strenuous activity, auto-oxidation of catecholamine ischemia-reperfusion/hypoxia (xanthine oxidase) because of restricted blood flow and activation of inflammatory cells as a result of injury or any infection (Gandhi and Gunjan, 2009). There also occurs an increase in metabolic rate during strenuous exercise requiring more oxygen consumption. The oxygen-uptake is many times higher than required because by the physiological process (deep breathing) excessive intake occurs as there is no filtering mechanism. The superfluous exercise oxygen-turned free radicals need to be scavenged as these are toxic moieties for cellular components. The body has an efficient antioxidant defense which scavenges the free radicals and thereby can inhibit their activity. However, if an imbalance occurs between the reactive oxygen/nitrogen species and antioxidant defense, may results into oxidative stress (Leewenburgh and Heinecke, 2001; Vollard et al., 2005).

The antioxidant defense comprises both, the enzymatic and non-enzymatic systems. The antioxidant enzymes include superoxide dismutases (SOD), glutathione peroxidases
(GSH), catalases (CAT) and the non-enzymatic are ascorbic acid, uric acid, bilirubin, glutathione, β-carotene, tocopherols (vitamin E), albumin, etc. (Powers and Jackson, 2008; Marciniak et al., 2009). In situations where the antioxidant defense gets compromised, any residual free radicals tend to cause oxidative modifications of cellular macromolecules (nucleic acids, proteins and lipids) and cause membranes and proteins to degenerate and induce damage to DNA (Hartmann et al., 1999; Cicek, 2006). Although the DNA repair system is efficient, yet these can remain unrepaired DNA. This residual DNA damage can cause cancer, atherosclerosis, myocardial infarction, cardiovascular and degenerative diseases as well as ageing (Uttara et al., 2009).

The role of oxidative stress therefore in causing genetic damage and disease, can in no way be undermined. Therefore in the following sections, literature on exercise-induced oxidative stress (2000-to present), lipid profile (as lipid peroxidation was assessed) of sportspersons (2001 onwards) and exercise-induced genetic damage has been reviewed.

The levels of 8-hydroxy-2'-deoxyguanosine(8-OHdG) activity of creatine kinase increased significantly for first three days in five well trained supra-marathon runners post-race but decreased significantly on day four compared to the values on the first three days (Radak et al., 2000). The authors concluded that adaptation to exercise (as after repeated exercise) in runners caused oxidative damage biomarkers and inflammation to decrease post-race.

In a study by Covas et al. (2002) on relationship between physical activity and oxidative stress biomarkers (lipid peroxides, superoxide dismutase and glutathione peroxidase) in 488 Spanish women, regression analysis revealed an association of low physical activity (≤6 metabolic equivalents, METs), with high activity of superoxide dismutase (p=0.002) and of high-intensity (>6 METs) physical activity with low or high glutathione peroxidase activity levels implying that physical activity has a modulatory effect on the activities of both the antioxidant enzymes.

Young male footballers (n=25; <21y) were investigated for oxidative stress (Metin et al., 2003) and it was observed that lipid peroxidation (as malondialdehyde (MDA) levels) MDA decreased in footballers aged under 21 when compared to values in
controls (p<0.001) while superoxide dismutase activity was significantly higher. A positive correlation was observed between Zn/Cu ratio and superoxide dismutase levels (p<0.05) and between maximum oxygen uptake (VO$_{2\text{max}}$) and superoxide dismutase (p<0.05). It was hence concluded that regular exercise could be beneficial against oxidative damage by reducing lipid peroxidation levels and increasing superoxide dismutase activity.

Sacheck et al. (2003) evaluated the effect of vitamin E supplementation on healthy young (n=16) and older (n=16) men doing eccentric exercise. In both groups post-exercise, there was a similar increase in levels of creatine kinase and iPF$_{2\alpha}$ (p<0.001) and of malondialdehyde (p<0.01) while the levels of 8-OHdG (oxidative DNA damage) were unaffected. However after Vit E supplementation, creatinine kinase levels decreased in the young men (p<0.05) and iPK$_{2\alpha}$ levels were suppressed in the older men while there was no direct influence of age as such.

Eighteen moderately-trained males were evaluated (Orhan et al., 2004) for oxidative damage using multiple biomarkers (eight aldehydes and acetone; o,o'-dityrosine) in urine samples (before one day and after three consecutive days of exercise). Significantly increased levels of urinary excretions of acetone (p<0.025), butanol (p<0.01), octanol (p=0.09), nononol (p=0.07), o,o'-dityrosine (p<0.025) and 8-OHdG (p=0.07) in the 12-hour day-time urine fraction were observed compared to values in the daytime fraction before exercise. A significant correlation was observed for training status with all other parameters, except for o,o'-dityrosine, showing post-exercise-induced oxidative damage in moderately-trained individuals.

In order to determine if a single bout of exhaustive exercise could induce oxidative stress, Tsai et al. (2004) assessed some biochemical parameters in blood samples of 22 rugby players performing exhaustive exercise starting at 6 km/hour for 3 minutes, followed by gradual increases until exhaustion. The levels of malondialdehyde, lactate and creatinine kinase were significantly increased and of superoxide dismutase decreased after exhaustive exercise. As the subjects consumed large amount of oxygen as well as anaerobic energy during exhaustive exercise oxidative stress was induced as evidenced by increased malondialdehyde levels and decreased superoxide dismutase activity in these well-trained rugby players.
Leelarugrayub et al. (2005) examined oxidative stress (malondialdehyde, protein hydroperoxide, glutathione and total antioxidant capacity levels) in athletes (n=20) and sedentary controls (n=20), before and after exhaustive exercise. The athletic group had higher total antioxidant capacity, lower protein hydroperoxide and malondialdehyde levels before exercise. A slight increase in glutathione and a significant reduction of total antioxidant capacity, malondialdehyde and protein hydroperoxide levels in both, sedentary and athletic groups, were observed after exercise. There was statistically more reduction of antioxidant capacity in sedentary group, concluding that the athletes with regular exercise had a beneficiary effect in terms of higher antioxidant capacity and lower protein and lipid peroxidation levels though a similar response to oxidative stress from exhaustive exercise was observed between sedentary and athletic groups.

Oxidative stress (Malondialdehyde+4-hydroxy2-(E)-nonenal, MDA+4-HNE), thiobarbituric acid reactive substance (TBARS) levels, creatine kinase (CK) and antioxidant parameters (glutathione peroxidase, superoxide dismutase and Vitamin C) in 19 female elite weight lifters and 17 non-athletic individuals were examined by Liu et al. (2005). The authors observed that there was increased oxidative stress and cell injury in athletes when compared to oxidative stress levels in non-athletes from long-term as well as after one week of intensive training.

Arslan et al. (2005) investigated serum metabolites of oxidative stress in three groups comprising a regular-exercise group, an acute exercise group and a sedentary group. The levels of paraoxonase 1 (PON1) activity, creatinine kinase and malondialdehyde significantly (p<0.001) increased in the regular-exercise group as compared to the values in the other two groups. A positive correlation between PON1 and malondialdehyde levels in the acute-exercise and regular exercise groups was also observed. It was hence concluded that regular exercise increased PON1 activity under the influence of oxidative stress.

Daud et al. (2006) conducted a study on sedentary healthy adults to assess the influence of cycling at different exercise intensities on antioxidant enzyme activities of catalase, superoxide dismutase (SOD) and glutathione peroxidase. A statistically significant increase in SOD levels (p<0.05) with an increased workload (VO₂max) was observed and
catalase activity was also affected by exercise intensity \((p<0.05)\). There was hence an increased reactive oxygen species production with an increase in exercise intensity, which probably induced the oxidative stress.

Demirbag et al. (2006), on investigating the acute effect of treadmill exercise test (TET) on oxidative/anti-oxidative biomarkers and genetic damage in 113 voluntary untrained subjects with suspected coronary artery disease, reported that total peroxide and oxidative stress index levels increased \((p<0.001)\) whereas total antioxidant capacity and vitamin C levels decreased after treadmill exercise test. The DNA damage was not however significantly elevated after the treadmill exercise test. The authors concluded that treadmill exercise test caused oxidative stress which, however, was not sufficient to cause DNA damage.

Male marathon runners \((n=25)\) on placebo \((n=14)\) or on allopurinol supplementation \((2\) hours before race, \(n=11)\) were assessed for the levels of malondialdehyde, NF-kB and xanthine oxidase (XO) activity before and after exercise (Gomez-Cabrera et al., 2006). Xanthine oxidase activity and malondialdehyde levels were increased \((p<0.05)\) after exercise when compared to before exercise levels, whereas this increase was prevented in runners on allopurinol. The authors observed that exercise-induced reactive oxygen species production acted as a signal for regulating molecular events in adaptation at cellular level in athletes and suggested that the administration of supplements before exercise should be revised, as these may prevent useful adaptation induced by exercise.

Half Ironman triathletes \((n=16)\) and full Ironman triathletes \((n=29)\) had significantly elevated \((p<0.05)\) malondialdehyde (MDA) levels after half and full Ironman races, whereas MDA levels were significantly lowered in half ironman triathletes when compared to control values (Knez et al., 2007). A significant decrease in antioxidant enzymes (GPx, CAT, SOD) was also observed after half \((p<0.05)\) and full \((p<0.001)\) ironman races.

The effects of aerobic and anaerobic exercises with similar workloads were investigated on some oxidative stress biomarkers in ten healthy male volunteers (Shi et al., 2007). Uric acid levels were increased significantly \((p<0.05)\) immediately after aerobic exercise, and between anaerobic and aerobic exercise, being higher in the anaerobic
group. After anaerobic exercise, there was a significant increase in 8-hydroxydeoxyguanosine and 4-hydroxy-2-nonenal at 24 hours and 3 hours, respectively. Overall, none of the exercises caused any apparent significant changes in the assessed biomarkers but suggested that exercise-induced reactive oxygen species formation was different in response to aerobic and anaerobic exercise. The authors concluded that oxygen consumption per se probably could not be a major cause of exercise-induced oxidative damage.

Margonis et al. (2007) examined the oxidative stress biomarkers response in 12 male athletes towards physical overtraining. The training consisted of five three-week periods (T1=2 tonnes/week, T2=8 tonnes/week, T3=14 tonnes/week and T4=2 tonnes/week), followed by a three-week period of complete rest. The training increased seven-fold in T3, which resulted in 56% increase in thiobarbituric acid reactive species (TBARS), 75% of urinary isoprostanes protein carbonyls and 96% of catalase as well as of glutathione peroxidase and oxidized glutathione, and a decline in reduced glutathione and antioxidant capacity compared to values in T1 and T2 periods. Correlation analysis revealed a significant positive association of isoprostanes and GSH/GSSG (glutathione/oxidized glutathione) levels with increased training volume and performance drop in athletes. These observations demonstrated that there was a marked response of oxidative stress biomarkers to overtraining, which could well be used for diagnosis of overtraining.

Oxidative stress in volleyball players (n=9), as an impact of exercise load (pre-competitive and in two competitive phases) was assessed (Neto et al., 2007). Glutathione reductase showed a significantly higher activity in all three phases when compared to controls. Catalase and glutathione reductase activities in phase three were significantly higher in comparison with the phase two values. Reactive carbonyl derivatives showed a significant increase at phase two when compared to values in both, control group (p<0.001) and phase one (p<0.05), followed by a significant decrease at phase three (p<0.001). No significant differences were observed for total sulfhydryl groups and thiobarbituric acid reactive species. There was lowest oxidative stress level combined with best performance during the principal phase (phase 3) of the championship.
The effect of a competitive soccer match on levels of oxidative stress and muscle damage markers in 16 soccer players (before 30 minutes, and after 24, 48 and 72 hours) revealed that the levels of myoglobin and total antioxidant capacity increased at 30 minutes, while creatinine kinase and malondialdehyde levels increased throughout the recovery period (p<0.05), when compared to pre-match values (Ascensao et al., 2008). A significant increase (p<0.05) of blood leucocytes and neutrophil counts, and a decrease of lymphocyte count (p<0.05) after 30 minutes of game were observed which returned to baseline levels during the recovery period. The authors suggested that the soccer match increased the levels of oxidative stress throughout the 72-hour recovery period.

Kelkar et al. (2008) reported that antioxidant supplementation (spirulina, an antioxidant drink) for two weeks prior to a marathon race (21 km), by eight male runners significantly (p<0.001) lowered malondialdehyde levels while a significant (p=0.000) improvement was observed for haemoglobin, packed cell volume and red blood cell levels in athletes prior to race. After the race, malondialdehyde levels were significantly lowered, and other indices showed only a marginal reduction. The authors concluded that antioxidant supplementation combated oxidative stress and improved the haematological status and performance in runners.

Superoxide dismutase, glutathione peroxidase and glutathione-S-transferase activities were significantly raised in basketball players (n=12) following regular long-term training (Melikoglu et al., 2008) compared to values in sedentary age-matched controls (n=11). The results of the study, therefore, supported that regular long-term training induced an antioxidant response.

Andersson et al. (2009) conducted a study on 16 elite female soccer players in response to 90-minute game to investigate the markers of oxidative stress [oxidized glutathione (GSH), GSH:GSSG and lipid peroxidation], dietary antioxidants (α-tocopherol, ascorbic acid, total carotenoids and polyphenols), uric acid and total glutathione (TGS). The results revealed exercise-induced acute increase (p<0.05) in GSSG, uric acid, TGS, α-tocopherol and ascorbic acid, whereas GSH:GSSG ratio and polyphenols decreased. Lipid peroxidation remained unchanged. It was concluded that intermittent exercise
induced a transient increase in oxidative GSH and reduced GSH:GSSG ratio as well as of endogenous and dietary antioxidant enzymes, which could prevent lipid peroxidation in players.

Aerobic and anaerobic exercise training with carnitine supplementation was studied by Bloomer and Smith (2009) on oxidative stress biomarkers (malondialdehyde, hydrogen peroxide and xanthine oxidase activity) in 32 healthy subjects. Oxidative stress was increased similarly in both aerobic and anaerobic power testing. After eight weeks of aerobic exercise and glycine propionyl-L-carnitine supplementation, malondialdehyde levels were lowered. There was no impact on hydrogen peroxide and xanthine oxidase activity at rest or after acute exercise. The study concluded that exercise training with glycine propionyl-L-carnitine supplementation had no effect on exercise-induced oxidative stress biomarkers.

Elite cross-country skiers (n=11), who underwent 18 days of endurance training, followed by 14 days of recovery period, were evaluated for antioxidant status before and after completing the training camp (Pialoux et al., 2009). There were six athletes who trained at 1200 meters and lived in hypoxia (at altitudes of 2,500m, 3,000m and 3,5000m) while five athletes comprised the control group who were trained and lived at 1200 meters. Ferric-reducing antioxidant power and Trolox equivalent antioxidant capacity, irrespective of the groups, decreased significantly (p<0.05 and p<0.01, respectively) after first day training (POST 1) and remained unchanged. Ferric-reducing antioxidant power levels returned to baseline after day 14 (POST 14) while lycopene and β-carotene levels decreased for hypoxia group and remained lower in POST 14. The study concluded that antioxidant levels remained low even after 14 days of recovery. Even after 18 days (POST 18) of high training and low training, there was no return to baseline levels.

In elite cyclists (37 males, 18 females), Lekhi et al. (2007) observed significantly increased concentrations of serum malondialdehyde (MDA), vitamins E and C (p<0.05), with higher superoxide dismutase (SOD) activity (p<0.001) and of uric acid level (p<0.01) but lower activity of catalase (p<0.05) due to exhaustive exercise when compared to values in sedentary controls (n=50). It was suggested that increased levels
of Vit E, Vit C and SOD activity were not able to counteract oxidative stress induced from exhaustive endurance training. The same elite cyclists had significantly decreased MDA levels on supplementation with Vit C (500mg/day) and Vit E (400IU/day) for two months (Gupta et al., 2009).

To evaluate exercise-induced oxidative stress and antioxidant status, Jose et al. (2009) conducted a study on 12 elite triathletes (7 males, 5 females). They observed significant increase in salivary uric acid (p=0.02) immediately after competition and salivary total antioxidant activity also increased significantly (p=0.001) than the level one hour before the competition. The lipid hydroperoxides level (an index of oxidative stress) however was significantly lowered than the level at one hour before the competition. The authors suggested that there was improvement in antioxidant capacity and lessening of the oxidative stress after exhaustive exercise.

In elite karate athletes (n=30), oxidative stress (levels of superoxide anion radical, \( \text{O}_2^- \) hydrogen peroxide, \( \text{H}_2\text{O}_2 \)) and antioxidant enzyme activity (SOD and CAT) were examined both, in resting condition and after the loading (Pesić et al., 2009). There was observed a significant decrease of \( \text{O}_2^- \) and significant increase of \( \text{H}_2\text{O}_2 \) after the load; CAT activity was also significantly elevated in athletes. It was hence concluded that oxidative stress was increased due to excessive physical load but not from the long-run physical training programme.

Teixeira et al. (2009) examined some dietary antioxidants (alpha tocopherol, Vit C and \( \beta \) carotene) activities of plasma enzymatic (SOD, Glutathione reductase and Glutathione peroxidase), non-enzymatic (TAS, Uric acid, Retinol lycopene, lutein+zeaxanthin) antioxidants and on the marker of lipid peroxidation (TBARS) and of muscle damage (creatinine kinase) in elite male kayakers/canoeists (n=17) and compared their values to those in age- and sex- matched sedentary individuals (n=17). In athletes, significantly higher levels of TBARS (p<0.001) and creatine kinase (p<0.011) were observed, with increased levels of antioxidants (\( \alpha \)-tocopherol, p=0.037; \( \alpha \)- carotene, p=0.003; \( \beta \) carotene, p=0.007) and of superoxide activity (p=0.002). The authors hence observed that despite higher antioxidant levels, the athletes had increased oxidative stress compared to controls which was increased from exhaustive exercise training.
The effect of regular exercise on oxidative and antioxidative parameters in 22 male wrestlers and 12 male sedentary controls was studied (Kürkçü et al., 2010). Statistical analysis revealed that the total antioxidant capacity (TAC), total peroxide concentration, total oxidant status (TOS), oxidative stress index (OSI) and dyslipidemia were significantly increased in wrestlers, suggesting that there occurred an increased oxidative stress as well as antioxidant capacity in well-trained wrestlers.

In 42 triathletes, after an Ironman race (3.8 km swim, 180 km bike-ride and 42.2 km run), Pinho et al. (2010) reported significant increases in TBARS levels (pre-race 1.15±0.11 and post-race 1.46±0.18 mmol/mg protein) and on lipid hydroperoxide (pre-race 0.75±0.03 and post-race 1.46±0.18 nmol/mg), protein carbonylation (pre-race 0.67±0.12 and post-race 20.15±0.60 mmol/mg protein), superoxide dismutase (pre-race 2.67±0.62 and post-race 3.97±1.48 U/mg protein) and catalase (pre-race 1.48±0.18 and post-race 2.84±0.39 U/mg protein) contents as well as of TNF-α, IL-6 and IL-10. These results implied significant alterations in oxidative stress and inflammatory parameters induced by Ironman race.

In a study (Bulduk et al., 2011) on 10 female volleyball players and 10 sedentary females, antioxidant and oxidative stress response after a 20-metre shuttle run test revealed significantly increased production of malondialdehyde levels and decreased glutathione and catalase levels in both groups. The authors stated that the persons doing strenuous exercise had vulnerability to increased oxidative stress.

Revan and Erol (2011) studied the effect of endurance training on exhaustive exercise-induced oxidative stress markers in male students undergoing training (n=12) and in a control group (n=12). The training group performed running exercise for 25-60 minutes/day, three days per week for eight weeks with 50-70% intensity. Plasma lipid hydroperoxide (LOOH) and the activities of glutathione peroxidase (GPx), catalase (CAT) and lactate dehydrogenase (LDH) were analyzed before and after eight weeks of exhaustive exercise. After exhaustive exercise, the levels of LDH were significant (p<0.05) higher in both control and training groups, whereas its activity was significantly higher (p<0.05) in control group, both at rest and after exhaustive exercises when compared to levels in the training group. Antioxidant enzyme activity (CAT...
level) was also significantly increased (p<0.05) after endurance training, resulting in prevention of lipid peroxidation (LOOH) implying that endurance training effectively prevented LOOH after exhaustive exercise.

Akkus (2011) conducted a study on 22 healthy young men and women who undertook two months of endurance training (cycling exercises for 60 minutes, four times a week) to investigate the effects of acute exercise and aerobic exercise training on oxidative stress biomarkers. The training increased the maximum oxygen uptake (VO\textsubscript{2max}) and the levels of TBARS, polycarbonyl and GSH were significantly altered in both males and females though the total superoxide dismutase activity in women increased. The author concluded that lipid and protein damage after acute exercise was not altered.

da Costa et al. (2011) studied oxidative stress and muscle damage in response to exercise in trained Brazilian junior soccer players (n=10). Levels of glucose, lactate, creatinine, urea, ascorbic acid, total plasma antioxidant potential, lipid hydroperoxides, malondialdehyde and creatine kinase were not altered during exercise, but a significant decrease (p<0.05) was observed in total antioxidant potential while a significant increase (p<0.05) was observed in malondialdehyde and creatine kinase immediately post-exercise. The authors concluded that increased altered oxidative stress was observed during first recovery stage after exercise.

Djordjenvic et al. (2011) conducted a study to establish the effect of long-term exercise training on oxidative stress in 33 young male handball players and compared it with that in 14 non-athletes. The athletes with poor aerobic power (VO\textsubscript{2max}<38.3 ml/kg/min) had highest levels of hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}) and lowest TBARS levels whereas the athletes with best aerobic power (VO\textsubscript{2max}>45.2 ml/kg/min) had lowest H\textsubscript{2}O\textsubscript{2} and maximum TBARS levels among all three groups (poor, average and good) of athletes. The athletes with average aerobic power (VO\textsubscript{2max} 38.4-45.1 ml/kg/min) had significantly higher levels of H\textsubscript{2}O\textsubscript{2} and TBARS (p<0.05) than non-athletes. Superoxide dismutase activity in athletes was also significantly higher (p<0.05) while catalase activity was lower compared to values in non-athletes. The authors stated that sports activities and aerobic capacity could induce changes in the redox status.
Dopsaj and coworkers (2011) examined the association of storage content of proteins (regulating iron transport) and the acute phase response with oxidative stress gender-wise in 138 athletes (73 females, 65 males). In females, linear model showed significantly higher values for reactive oxygen metabolites (p=0.030), superoxide dismutase (p=0.001), lipid hydroperoxides (p<0.001), pro-oxidant antioxidant balance (p=0.002), advanced oxidation protein products (p<0.001) and superoxides (p<0.001) compared to values in the male counterparts indicating the higher susceptibility to oxidative stress in females. Transferrin and ferritin proteins and acute phase reactants were negatively related to oxidative stress implying that ferritin level variation could be contributing to oxidative stress in females.

The association of military basic training with levels of oxidative stress markers and antioxidant status (Tanskanen et al., 2011) in 35 males on an eight-week basic training, revealed that the ratio of oxidized to total glutathione (GSSG/TGSH) and GSSG decreased with increased daytime moderate-to-vigorous physical activity. Also, at every time point of basic training, TGSH decreased, the GSSG and GSSG/TGSH levels increased whereas antioxidant capacity decreased after four weeks in training subjects. The overreaching training (n=11) subjects had higher GSSG, GSSG/TGSH and MDA (p<0.01-0.05) levels at rest whereas there was lower response to exercise compared to non-overreaching subjects. It was suggested that there was an association of overreaching training with increased oxidative stress.

Eighteen male football players who performed the 30s-Wingate test (a short maximal exercise) had significantly increased level (p<0.001) of white blood cells mainly comprising monocytes, neutrophils and lymphocytes. Uric acid and total bilirubin levels were increased as was total antioxidant status after the exercise (Hammouda et al., 2012). The results substantiated that short-term maximal exhaustive exercise could induce oxidative stress.

Kiyici and Kishali (2012) studied 18 soccer players and reported a significant increase (p<0.05) in superoxide dismutase and catalase levels at the beginning of the training period whereas no change was observed of malondialdehyde levels. At the end of ten consecutive training programmes, serum catalase activity decreased and
malondialdehyde levels were increased (p=0.05), indicating that there was an increased reactive oxygen species production which caused lipid peroxidation by exhausting the antioxidant defense system.

Radovanovic et al. (2012) observed no changes in the oxidative stress parameters of malondialdehyde, catalase, carbonyl and sulphhydryl groups and total antioxidant status (TAS) examined during four weeks pre-competition training programmes in ten male judokas, suggesting that the pre-competition training period-pattern had no effect on well-trained judokas.

In elite female water polo athletes, Varamenti and co-workers (2012) observed that in different phases there was increased level of oxidative stress (thiobarbituric acid reactive substances, protein carbonyl). Variation in inflammation (plasma monocyte chemoattractant protein-1 and interleukin-10) was also observed. These changes were observed to occur throughout the season.

Tong et al. (2012) studied serum oxidant (thiobarbituric acid reactive substances, TBARS) and antioxidant parameters (XO, CAT, GSH, SOD, T-AOC) in 12 cyclists, 12 runners and 12 untrained adolescents. The levels of XO, GSH and CAT were significantly elevated in cyclists on comparison with the levels in runners and in controls. In runners, CAT levels were increased compared to those in controls. The authors stated that blood redox balance was partly from an adaptive endogenous process which probably was the result of habitual intake of antioxidant nutrients as observed in the case of adolescent athletes of the study.

Zanella et al., (2011) evaluated lipid profile (LP), apolipoprotein A-I (apo A-I) and malondialdehyde (MDA) in foot-ballers (FG, n=20) with sedentary individuals (CG, n=20) whether they have any relationship with physical exercise by comparing the groups of and their relatives (60 RFG and 57 RCG). FG showed lower levels of total cholesterol, LDL-cholesterol fraction, apo A-I, and higher level of HDL-cholesterol fraction (HDLc) compared to RFG. Moreover, FG had reduced levels of MDA compared to CG and RFG. These results suggest an association between physical exercise and lower levels of MDA in FG. Therefore according to author, physical
activity seems to promote beneficial effects on the lipid profile regardless of the genetic influence considering HDLc levels.

Gokhan (2013) studied the levels of total antioxidant capacity, total oxidant status and blood lipoproteins in volleyball players (n=20) and compared with levels with those in sedentary controls (n=32). The results were significantly increased (p<0.05) in players for TAC, TOS and LOOHs when compared to controls, whereas no difference was observed for lipoproteins. Thus the author concluded the oxidative stress in players resulted from increased oxygen consumption during sport/regular exercise.

In young basketball players of different ages viz. group IV (15y), V (16y) and VI (17y), levels of malondialdehyde and hydrogen donors were determined and the values were compared to those in age-matched control groups (Group I, II, III) by Kollos and Tache (2013). The levels of MDA increased with age, being highest in group VI with decreasing levels of hydrogen donors. These observations demonstrated that changes in oxidant/antioxidant balance occurred in individuals on regular training.

2.3 Studies on Lipid Profiling of Sportspersons

Exercise has the potential to induce changes in the lipid profile and thereby reduce the risk of diseases associated with abnormal lipid profile. Some studies on this aspect (2005 onwards) is reviewed here.

Gandapur et al. (2006) studied the lipid profile and apoprotein B levels in 53 subjects who had been doing regular exercise (24 civilians and 29 army men) for the past six months and in 39 sedentary workers. Total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), apoprotein B and cholesterol/high-density lipoprotein ratio of control group showed significant differences when compared to values in the total exercise group as well as to the values in the civilians group. The decreased levels of apoprotein B, low-density lipoprotein and total cholesterol/high T density lipoprotein ratio indicated the beneficial effect of regular aerobic exercise.

Manna et al. (2006, 2009) studied the training induced changes on different physiological and biochemical parameters in 30 Indian field hockey players and 30
Indian male soccer players regularly playing competitive their respective sports. A significant decrease (P<0.05) in body fat, and a significant increase (P<0.05) in LBM following both 6 wks and 12 wks of training was observed. A significant reductions (P<0.05) were observed in hemoglobin, total cholesterol, triglyceride and LDLC after the training whereas hand plasma levels of urea, uric acid and HDLC were increased significantly (P<0.05) following the training in players of both sports. The author concluded that a decrease in body fat and the plasma levels of cholesterol as well as LDLC and increase in HDLC is beneficial for good health and better performance.

Chatterjee et al. (2007) determined the plasma lipid and lipoprotein profile of Indian women boxers during pre- and post-training camps of six weeks’ duration. There was significant decline (p<0.001) observed in cholesterol, LDL-cholesterol, HDL-cholesterol levels post-test. The author concluded that women boxers on regular training had a favorable lipid profile.

In the lipid profiles of 12 national gymnast’s athletes and 20 healthy controls (Ata et al., 2008) there was significant increase in HDL cholesterol (p<0.05) and decrease in levels of total cholesterol, glycerides and LDL-cholesterol in male and female athletes compared to levels in controls. The authors suggested that exercise was beneficial in the regulation of lipid metabolism.

de Souza e Silva et al. (2009) conducted a study on 45 male Brazilian military police academy members, randomly assigned to three groups- aerobic fatmax zone training (FG, n=18), traditional military training (TM, n=15) and a non-training control group (C, n=12). A significant increase in HDL (p<0.01) and decrease in LDL (p<0.001) levels was found only in TM group compared to those in the C group; the Post-to-Pre training ratios (p<0.005) in the FM group for TC, TG and HDL levels were also significantly increased (p<0.010).

Witek (2009) studied the lipid profile and assessed creatine kinase levels in 14 Polish elite volley ball players during various phases of the competition period. There was a gradual increase in total cholesterol, low density lipoproteins, total cholesterol to high density lipoprotein ratio and low density lipoprotein to high density lipoprotein ratio while high density lipoprotein decreased. All the values were in the normal range.
Yates et al. (2009) investigated the lipid profile of 36 active national football players categorized into one group (n=20) which was on treatment with Omega-3s and the other group was the control (n=16). The lipid profile of the first group was improved (though not significantly) as there were increased high density lipoprotein (HDL) and decreased triglycerides, VLDL, LDL, remnant lipoprotein and VLDL protein levels. There were also observed improved levels of docosahexaenoic acid (106.67%) and eicosapentaenoic acid (365.82%) showed improvement in the first group. On the basis of these results, the authors recommended that Omega-3s be given to all players and to those who are active in sports since the risk for CVD in football players increases with increasing age.

Manna et al. (2010) conducted a study on 120 male field-hockey players appropriated as under 16 year (14-15 years), under 19 year (16-18 years), under 23 year (19-22 years) and senior (23-30 years) groups. On the basis of three phases of training sessions comprising a transition phase, a preparatory phase and a competitive phase, the changes in biochemical variables in these players with reference to age and training were studied. Hemoglobin levels showed a significant (p<0.05) reduction, and serum urea, uric acid and high-density lipoprotein-cholesterol after training were significantly increased whereas total cholesterol, triglycerides and low-density lipoprotein-cholesterol levels decreased in preparatory and competitive phases in comparison to those in the transition phase. However, all the biochemical parameters were significantly increased as a function of age.

To investigate the lipid profile, Bananeifar et al. (2011) carried out study in male athletes’ college student and non-athletes. The blood samples were collected to determine the levels of plasma total cholesterol, triglycerides, low density lipoprotein, apolipoprotein B and high density lipoprotein. The results revealed significantly lower levels of plasma triglyceride, total cholesterol, low density lipoprotein, TC/HDL and apolipoprotein B (aPOB) in athletes group was lesser than non-athlete group and high density lipoprotein significantly higher levels in athletes group in compare non-athletes. The comparison between variables aPOB & LDLc also indicated significant relation in athlete’s group. Therefore, the study shows that the regular physical activity helps in prevention of cardiovascular disease.
In some athletes (11 walkers and 11 boxers) and in sedentary controls (n=11), Purohit et al. (2012) reported higher HDL-cholesterol and lower LDL-cholesterol levels in walkers and boxers compared to levels in sedentary subjects. The best levels of Cholesterol/HDL ratio, LDL-cholesterol and HDL-cholesterol were observed significantly in walkers, thereby implying that walking, as a regular physical activity, provided an advantage in improving the lipid profile.

Sanghavi et al. (2012) studied the effect of regular physical exercise on lipid profile in sports persons and compared the results with sedentary persons. The result revealed significantly increased levels of total serum cholesterol, Low density lipoprotein cholesterol, Very low density lipoprotein and Serum Triglyceride in sportspersons and high density lipoprotein cholesterol showed significantly lower values in control subjects when compared with the sports persons. The author concluded that regular physical exercise in the form of sports, aerobics or workouts leads to more favorable cardio-vascular risk factors profile that improves the quality and duration of life.

To investigate the effect of aerobic exercise (running) performed regularly for eight weeks without a special diet on blood lipid and lipoprotein levels, Saritaş (2012) conducted study on 20 non-smoker, moderately active volunteer with ten training Group and ten control group. Training group performed aerobic exercise at target heart beat rate of 60 to 70% for 1 h/day for 4 days per week during 8 week-trial. There observed increased plasma levels of low density lipoprotein-cholesterol (LDL-C) in training group and decreased in control group, while levels of high density-cholesterol (HDL-C) decreased in both groups being statistically significant only in training group. In conclusion, a short term (8 weeks) aerobic exercise program performed without a special diet in moderately active young men may be considered as insufficient to make favorable effects on blood lipid profile.

In 22 female professional volleyball players, Mielgo-Ayuso et al. (2013) analysed lipid profile and observed decreased LDLc levels and both atherogenic indices in the players (p<0.05) compared to the values obtained at base line. The authors concluded that data indicate that the activity of the female professional volleyball players was healthy by heart as their lipid profile improved, despite an inadequate intake of fats in their diet.
2.4 Studies on Genetic Damage Due to Strenuous Physical Activity

The association of strenuous physical activity and genetic damage was first reported by Tice et al. (1990) who observed increased DNA damage in one of the three volunteers after a five-kilometer run. Since then a number of studies on persons involved in strenuous activity either professionally, for keeping fit or as required by occupation have been similarly investigated. The literature on genetic damage from intensive physical activity is reviewed here.

Inoue et al. (1993) studied the effect of physical exercise on nine swimmers and nine distance runners. There was observed a statistically significant decrease in 8-OH-dG content in nuclear DNA after intermittent swimming though the differences in runners was not statistically significant. However, the ratio of hypoxanthine to creatinine increased and levels of xanthine and uric acid decreased significantly however in both the groups after exercise, suggesting that those was exercise-induced adaptive response in both the groups.

Niess et al. (1996) assessed DNA damage using the single cell gel electrophoresis (SCGE) assay in six trained (TR) and five untrained (UTR) men after exhaustive exercise. A significant increase in DNA migration 24h post-exercise was observed in both the trained and untrained men. The damage was however significantly lowered in TR (18.7±6.8%) when compared to levels in UTR (35.7±8.9%) men. The authors observed that exercise-induced adaptation to training mitigated and lower the DNA damage observed in trained men.

Blood cultures of six healthy volunteers, before and after two consecutive sprints, showed a significantly increased frequency of micronuclei in five subjects with culture initiation 24 hours after physical workout while the culture of one subject after 48 hours of the workout, also had significantly increased micronuclei frequency (Schiff et al., 1997). There was also observed a sharp increase in lactate concentrations after the sprints. The authors concluded that blood lymphocytes sustained severe mutations at chromosomal levels after exhaustive physical exercise.

Eleven long-distance male runners, six untrained males and eleven long-distance male runners with different exercise regimen, showed no changes in 8-OHdG concentrations,
pre- and post-exercise (Sumida et al., 1997) suggesting that accumulation of oxidative DNA damage did not occur after a single bout of exercise.

Similarly, Asami et al. (1998) observed a reduction of 8-hydroxyguanine (8-OHdG) levels and significantly increased repair activity in untrained subjects (n=13) whereas no changes were observed before or after exercise in trained men (n=10), suggesting that physical exercise could be a beneficiary tool for reducing oxidative DNA damage in leucocytes.

Hartmann et al. (1998) examined the effects of short distance triathlon on the induction of DNA effects in peripheral blood leukocytes, oxidized DNA bases and micronuclei (MN) frequency in six athletes (three males and females each). DNA migration (tail moment) increased in all individuals in a biphasic manner after exercise, i.e. DNA migration levels elevated 24 hours post-exercise and lowered 48 hours post-exercise. The maximum increase was observed 72 hours post-exercise with baseline values elevated even after 120 hours while 9-hydroxy-2-deoxyguanosine levels and micronucleus frequencies after exercise showed no differences. The authors concluded that increased DNA migration, suggesting their data repaired error-free and did not result in chromosomal damage.

A single bout of intensive running on a treadmill for 30 minutes by trained and untrained university students (Umegaki et al., 1998) did not significantly increase lymphocytic chromosomal damage in both the groups. However on X-ray-irradiations (1.5 Gy dose) of in vitro lymphocyte cultures, chromosomal damage (MN) was significantly increased in the untrained group but not in the trained group. It was suggested that intensive exercise caused a very slight increase in chromosomal damage in the untrained group which was increased by secondarily–induced oxidative stress as a result of X-ray irradiations.

Healthy subjects, after a single bout of exhaustive exercise as a maximal bicycle exercise test at high altitude hypoxia (4,559 m for 32 days), had increased urinary excretion of 8-oxod-G during first day while there were more endo III-sensitive sites on day three; DNA strand breaks were also observed to be more at high altitude than at sea level (Moller et al., 2001). Exercising induced more damage in hypoxic condition as
compared to that in normal condition. The authors concluded that reactive oxygen species generated during mitochondrial respiration leakage or during hypoxia-induced inflammation, besides the depleted capacity of antioxidant defense system reduced by exhaustive exercise, could probably be causing the observed DNA strand breaks and the oxidative DNA damage.

Massive aerobic exercise (42 km marathon race) by male runners induced DNA single strand breaks whose frequency increased gradually after the race (p<0.001) and remained at the same level until two weeks later (Tsai et al., 2001). Oxidized pyrimidines (endonuclease III) increased post-exercise; also a two-fold increase occurred, each in urinary 8-OHdG and creatinine kinase (CK) levels. Creatinine kinase and lipid peroxidation metabolites further showed a significant correlation with oxidative DNA damage. These results implied that massive aerobic exercise caused oxidative DNA damage (prominently on pyrimidines) which remained as such up to one week after the race.

Levels of DNA fragmentation and apoptotic cells in the plasma-rich leucocyte layer in athletes were elevated as compared to values in non-athletes (Korraa et al., 2002). The frequency of micronuclei was however not significantly different in non-smoker athletes and non-smoker controls while smoker athletes had significantly higher micronuclei frequency when compared to the frequency in control smokers. The authors concluded that though no severe toxicity was induced by exercise, yet exercise and cigarette smoke individually induced oxidative stress which probably caused the observed genetic damage.

Radak and co-workers (2003) reported an increased activity of 8-oxoG DNA glycosylase (hOGG1) in skeletal muscles but not of the repair enzyme after a marathon race in six trained male physical education students. The authors suggested that the upregulation of repair enzymes could be an adaptive response to regular exercise.

Mooren et al. (2004) conducted a study on 16 volunteers after a marathon run to investigate the effect of training status on exercise-induced apoptosis as well as on the expression of cell-death receptors and ligands. There was an early increase in percentage of apoptotic cells after the marathon race, followed by a significant decrease
after exhaustive treadmill test, and after the marathon in badly-trained athletes. The authors concluded that exercise-induced lymphocytic apoptosis depended on the training of the athletes, because in badly-trained athletes, cell death was induced while there were no changes in highly-trained athletes.

Mastaloudis et al. (2004) studied the effect of antioxidant supplementation on DNA damage using the comet assay in 21 runners during a 50 km ultra-marathon race and observed no significant differences for DNA damage in the male groups, on or without supplements. However in women runners taking antioxidants, DNA damage was significantly (p<0.008) reduced by 62% compared to those on placebo. It was concluded that endurance exercise induced DNA damage at mid-race and antioxidant supplementation enhanced the recovery of damage in women runners.

Briviba et al. (2005) on investigating half-marathon and full-marathon runners (before and after the runs) for DNA damage and antioxidant capacity, reported a significant increase in the levels of oxidative DNA damage (oxidized pyrimidines) using the comet assay in lymphocytes, though antioxidant capacity was unchanged. The granulocytes and monocytes however generated oxidative burst after the race. Natural killer cells also increased at the end of the half-marathon race. The authors suggested that oxidative DNA damage in lymphocytes probably resulted from the decreased antioxidant capacity and the increased formation of reactive species by phagocytes probably caused a moderate increase in oxidative damage during high intensive exercise.

The comet assay was performed on peripheral blood lymphocytes of rickshaw-pullers, as rickshaw-pulling entails strenuous physical activity (Pandey et al., 2006). A significant increase in mean Olive tail moment (p<0.001) was observed in comparison to the values in healthy controls, implying that strenuous physical activity induced DNA damage in peripheral lymphocytes.

Peters et al. (2006) on investing lymphocytic DNA damage (using the SCGE assay) and apoptosis (using flow cytometry) in well-trained endurance athletes (runners), observed no significant differences when values were compared for before, immediately after, and 3h after treadmill running at 75% VO2max.
Body-builders (n=15) performing strenuous workouts in gymnasiums were investigated for chromosomal damage (clastogenicity/aneugenicity) in their peripheral blood lymphocytes (Gandhi and Mahajan, 2007). There was observed significantly increased percentage frequency of micronucleated cells in body-builders compared to values in sedentary normal healthy controls (n=10). The extent of DNA damage was influenced by the daily exercise durations, time since-exercising and the warm-up schedule.

In wrestlers (n=15), Gandhi and Kumar (2007) also observed significant increase in lymphocytic micronuclei frequency compared to values in controls (n=10). The frequency of micronuclei increased with age, daily duration and longer routine of exercising.

Reichhold et al. (2008) conducted a study in 20 male triathletes to investigate the effect of ultra-endurance exercise on DNA stability using the cytokinesis block micronucleus cytome assay. The number of micronuclei decreased (p<0.05) after the race and declined further at 19 days’ post-race (p<0.01). The frequency of nucleoplasmic bridges declined from 2 days’ pre-race to 19 days’ post-race (p < 0.05) while the frequency of nuclear buds increased up to 5 days’ post-race (p<0.01) and declined to baseline values, 19 days after the race (p<0.01). The authors suggested that there was no long-lasting genetic damage in well-trained athletes and that upregulation of repair mechanism occurred, preventing severe oxidative stress and DNA damage even after strenuous exercise.

Gandhi and Chopra (2009) assessed genetic damage in peripheral blood leucocytes of healthy individuals (n=40) following a regular gymnasium regimen to keep fit and compared it with that in healthy sedentary individuals (n=15). The physically-active males (p<0.001) and females (p<0.05) had significantly higher values for mean DNA migration when compared to values in control males and females. The percentage of cells with tails as well as DNA migration in females was significantly higher (p<0.001) in the physically-active group. VO_{2max}, length of time following an exercise regimen and warm-up duration in physically-active females showed a correlation with DNA damage; in the males the first two factors also showed a correlation with DNA damage.
indicating that DNA damage was induced by strenuous exercise in individuals following a fitness routine to keep fit and healthy.

Reichhold et al. (2009) reported that DNA strand breaks (on SCGE assay) decreased significantly (p<0.05) immediately after an Ironman triathlon (an ultra-endurance exercise), but increased (p<0.01) a day after the race and again declined five days after the race in 28 well-trained male triathletes. Concurrently, the total antioxidant capacity increased while apoptosis and necrosis (CBMN assay) decreased significantly (p<0.01) immediately after the race. The authors observed that the induced DNA damage in lymphocytes of these well-trained athletes lowered within 19 days of the race.

In young men (trained, n=8; untrained, n=8), Tanimura et al. (2010) examined the effect of three consecutive days of one hour high intensity exercise on lymphocytic count, oxidative DNA damage and apoptosis. Lymphocyte count decreased significantly in untrained men at day four compared to values at day one. However the count remained unchanged in trained subjects though there was a significant (p<0.05) increase in oxidative DNA damage in both groups (trained and untrained) at day four after high-intensity exercise. No significant changes were observed for serum LPO, superoxide level, CD95+, Annexin-V+ lymphocyte cells and serum cortisol concentrations in both groups. It was concluded that there was increased genetic damage after exhaustive exercise.

Sardas et al. (2012) assessed DNA damage (using the comet assay) and the effect of vitamin E supplementation on exercise-induced oxidative DNA damage in rowers (n=12) and physical education students (n=11). Per cent DNA was significantly higher in rowers for pre-exercise values when compared to the values in physical education students. After the exercise, the percent tail DNA increased significantly (p<0.001), both in rowers and physical education students. Vitamin E supplementation for 60 days resulted in significant (p≤0.001) decrease in per cent tail DNA from the initial pre-supplementation values.

Atli (2013) determined the plasma total antioxidant status, total oxidant status, oxidative stress index and peripheral lymphocyte DNA damage in 25 adult football players and in 25 sedentary controls. There was a significant increase (p<0.001) in antioxidant
capacity and decrease in oxidative stress and of DNA damage as well as of total oxidant status and oxidative stress index in football players compared to the respective values in controls.

College-going male wrestlers, randomly selected under placebo (PL) (maltodextrine powder, n=16) and on creatinine monohydrate (CrM) (n=15) supplementation were assessed for oxidative DNA damage (8-OHdG) and lipid peroxidation (8-isoprostane, 8isoPGF$_2\alpha$) by Mirzaei et al. (2013). Significant (p<0.05) 24h post-exhaustion before supplementation in both groups increased 8-OHdG levels (13.36%CrM and 24.08%PL) though lipid peroxidation levels were not increased. After seven days of supplementation, there occurred a significant decrease of 8-OHdG 24h post-exercise in CrM (32.65%) levels compared to the levels before supplementation and in levels in the placebo group at 24 h post-exercise. The authors concluded that CrM supplementation reduced the oxidative stress induced by exercise in wrestlers.

2.5 Genetic Polymorphisms and Sports Performance

Though sports performance improved with intensive and prolonged training, good coaching and strong psychology, the genetic endowment is also known to contribute towards it being independent of polymorphisms (Calo and Vona, 2008). A number of studies have shown association of endurance performance with genetic polymorphisms especially of the angiotensin converting enzyme gene (ACE); β-adrenergic receptor gene (β-ARDB1), methylene tetrahydrofolate reductase (MTHFR), Bradykinin receptor (BDKRB2), α-actinin-3 (ACTN3), Peroxisome proliferator-activated receptor alpha (PPARα) and Nitric oxide synthase (NOS). Some studies from 2005 onwards demonstrating the association of genetic variants with sports performance are reviewed here:

On a total of 80 elite athlete (18 skiers, 12 triathletes, 15 soccer and 35 hockey players) and 37 juniors, Vedyakov and Tonevitskii (2006), investigated whether the genetic variants of CYP4501A1, GSTT1, GSTM1, MnSOD MTHFR and ACE) play a key role in metabolic processes in the body during strenuous exercise. The frequency of the GSTM1 deletion genotype was 49% of the detected GSTT1 was 17% and homozygous wild of GSTP1 (313) was %, heterozygous was % and of GSTP1 (341) homozygote
mutation was 18%. The genotype Ala/Ala of SOD was 56%, of Ala/Val 20% and Val/Val was 24%.

The Arg16Gly SNP of β2-adrenoceptor gene was studied for its association with endurance performance in a case-control study (Wolfarth et al., 2007) comprising 313 white male elite endurance athletes and 277 white male sedentary controls. The athletes belonged to Germany (n=186), North America (n=76) and Inland (n=52) competing in cross-country skiing (n=104), biathlon (n=86), cycling (n=71), running (n=38) and in triathlon and rowing (n=14). Though genotypic distribution in both groups was in Hardy-Weinberg equilibrium, genotypic differences were significant with Arg16 higher in athletes (p=0.030). However the allele frequencies and genotype distributions as functions of sports, places of origin or anthropometric data (in both groups) did not differ. The authors suggested that Arg16Gly polymorphism could be associated with endurance performance in white males.

In the Genathlete study, Wolfarth et al. (2008) conducted research on 316 elite endurance male athletes with a VO_{2\text{max}}>75 \text{ ml/kg} and on 299 unrelated sedentary control males with VO_{2\text{max}} values below 50 ml/kg and examined three polymorphisms [(CA)_n, 27 bp rpt, Glu298AspSNP] of endothelial nitric oxide synthase (NOS3) gene within the athletic groups. No differences in allele frequency or for places of origin were observed. Genotype distributions for Glu298Asp of NOS3 and for 27 bp CA repeat marker were in Hardy-Weinberg equilibrium and allele and genotype frequencies of Glu298Asp and 27 bp repeat markers did not differ between athletes and controls. However on comparing carriers with non-carriers for NOS3 (CA)_n repeat allele, a statistically significant excess of 164 bp allele of (CA)_n repeat was observed in elite endurance male athlete cohort (p=0.007), implying that despite the fact that it is located in an intron (intron 13) as an indirect marker, it may be responsible for some of the differences between elite endurance athletes and sedentary controls.

Hui and Hui-qin (2009) investigated for an association of glutathione-S-transferase P1 (GSTP1) genetic polymorphism with human exercise capacity in 86 professional Tibetan mountain climbers. The variant genotypes (A/G+G/G) were significantly lower in climbers compared to the number in control subjects (p<0.01). The exercise capacity in
climbers with variant genotypes was decreased by 119 times compared to that in climber with the wild-type genotypes, implying that the subjects with wild-type genotype correlate with more exercise capacity in high altitude environment and so have exercise predominance.

In Asian Indian athletes (n=155) and 150 sedentary controls, Kothari et al. (2011) evaluated the association of α-actinin 3 gene genotypes (ACTN3 R577X) with power-based performance and endurance abilities. However there were no significant differences in allelic frequencies (R/X) between the two groups. On the basis of athletes grouped as international/national (n=72) and regional (n=83) competitive levels, the frequency of the R allele was significantly associated (p<0.01) with power-sporting ability compared to that in the total athletic group; also the frequency of X allele was higher (but was not significant at p<0.07) in endurance athletes. Furthermore though a gender effect with respect to frequency of XX genotype was apparent in female power and endurance athletes, yet because of small number of participants no associations can be made.

Cieszczyk et al. (2012) examined the association of the ACTN3 genotype with athletic performance in 83 male (37 elite and 46 non-elite) Polish runners (national competitors) and 204 unrelated controls. The athletes had the genotypic distribution: 53.8% RR, 38.8% RX, 7.4% XX DD which differed significantly (p=0.01) to that of controls (36.3% RR, 46.1% RX, 17.6% XX). The 577 R allele was also significantly higher in the elite (75.7%, p=0.05) and non-elite (71.7%, p=0.06) rowers compared to that in controls (59.3%) but there were no differences between the two categories of rowers for both, allele and genotypic frequencies. The authors concluded that the ACTN3 R577X polymorphism has a role in rowing capacity as was predominant in rowers though it did not bestow a beneficial effect on endurance performance and hence caution is required in the use of this polymorphism as a genetic marker for rowing talent.

The distribution of the ACTN3 (R577X) and ACE (D/D) polymorphisms in Italian 59 elite male athletes (17 gymnasts, 12 runners and 33 soccer players) and 31 controls (Massidda et al., 2012) revealed that the ACE allele and genotypes did not differ between the groups, though the DD genotype and D allele had higher frequencies. In the
case of ACTN3 genes, there was a significant difference only between elite gymnasts and controls (p=0.03) with absence of XX genotype and excess of RR genotype. No association of this polymorphism with runners or soccer players was however observed. The authors therefore concluded that the ACTN3 RR genotype is determinant of elite gymnastic status but not for soccer or track events.

Hong and Jin (2013), on analyzing ACTN3 genetic polymorphism for elite athletic performance in 150 elite Korean athletes and 361 random controls, reported no significant association for genotypic or allelic frequencies between sprint/power athletes (SPA=84) and controls, and between endurance/power athletes (EPA=66) and controls. However the ACTN3 R577X polymorphism showed an association with athletic status in female SPAS and in female controls (p=0.028), between SPA and EPAS (p=0.009), and between EMPS and controls (p=0.016). The Q523R polymorphism also was similarly distributed in this group. The authors concluded that their results implied a significant influence of sex-specific ACTN3 R577X genotype on the elite Korean female SPAS-status.

2.6 Gene Polymorphisms and Genetic Damage

The biotransformation of foreign substances within the body takes place in two phases: phase I and phase II. In phase I, including cytochrome P450 enzymes, which transform parent compounds transformed into polar metabolites. The phase II includes transferases viz. glutathione S-transferases (GSTs), N-acetyltransferases (NATs), sulfotransferases (SULTs) and others which bio-transform endogenous compounds and xenobiotics to easily excreatable forms (Jancova et al., 2010). In the present study, genotyping of three variants of GST and two of SOD2 has been carried out. Therefore some background information on these genes is presented here.

The Glutathione S-transferases (GSTs) are important enzymes encoded by GST genes. They have a protective against reactive and toxic electrophiles as reactive oxygen species, which arise from normal metabolic processes and are also those formed by cellular oxidative reactions (Jancova et al., 2010). The polymorphisms in GST genes can alter the protein function/expression of the encoded enzymes resulting in cellular toxicity; many of these polymorphisms were associated with various types of cancers.
(Dusinska et al., 2012). The human cytosolic GSTs are classified into eight groups. These with their genes are: alpha, mu, pi, theta, zeta, omega, kappa and microsomal (Terada, 2005). During detoxification reactions, polymorphic states of these metabolizing enzymes have a role in the inter-individual differences which can modulate the effect of chemical carcinogens (Norppa, 2004). The GSTT1 and GSTM1 deletion variants have no enzyme activity with the result that there is retention of the reactive intermediates produced in phase I detoxification of xenobiotic metabolism; these are often toxic and/or harmful. There is decreased enzymatic activity in the GSTP1 allelic variants, viz. G313(Ile/Val) and G341(Ala/Val) (Vedyakov and Tonevitskii, 2006). The G313 variant presents a substitution polymorphism in exon 7 that results in a substitution of Ile by Val (became of nucleotide substitution of adenine by guanine (A313G) at position 105 Val (Ile105Val). In the G341 variant (Ala/Val), cytosine to guanine substitution causes Ala to be substituted for Val at ninth amino acid (Ala-9-Val). This leads to decreased activity of the GSTP1 enzyme and there is retention of the aggressive products of phase I detoxification.

**Superoxide Dismutase 2, mitochondrial** (SOD2), the product of SOD2 is an antioxidant enzyme that localizes to the mitochondria and its function is to reduce the free radicals in the cell by detoxification of superoxide anions to hydrogen peroxide and oxygen, thereby reducing the hazard of oxidative stress in the cell. The presence of SOD2 in mitochondria can influence the latter role as a source of reactive oxygen species (ROS) generation as well as a source of ROS removal (Clair, 2004). In fact in the MnSOD knockout-mice, there was reported increased oxidative DNA damage (Melov et al., 1999). The SOD2 gene is composed of five exons and four introns and is localized at chromosome 6q25. The gene has two variants Ala9Val and Ile58Thr. The C → T substitution (C47T) results in an Ala to Val change at the ninth position (Val-9Ala); this Ala to Val change alters the secondary protein structure and the altered protein fails to dismutase superoxide anions and so ROS are not neutralized. Another polymorphism (Ile58Thr) in exon 3 affects the stability of SOD2 and reduces the amount of protein thereby also causing a reduction in the activity of the enzymes. and subsequently there is increase in ROS production. Remmen et al. (2003) had suggested
that reduced SOD activity could increase the susceptibility to cancer as the Ile58Thr mutation in the SOD gene altered the structure of Thr58 polypeptide. This caused SOD to occur as a dimer in solution with lesser activity and decreased thermo stability compared with the MnSOD formed from the wild type Ile58 polypeptide.

Some studies on GST and SOD2 genes having association with genetic damage and oxidative stress in individuals exposed to different occupational exposures or with any disease are tabulated below:
<table>
<thead>
<tr>
<th>Gene</th>
<th>Type of Marker Genetic Damage/Oxidative Stress</th>
<th>Study Group</th>
<th>Assay performed</th>
<th>Outcome</th>
<th>Reference</th>
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<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Genetic damage</td>
<td>Chinese workers exposed to 1,3-butadiene</td>
<td>SCE, CBMN</td>
<td>GSTT1(-) with ↑ MN GSTM1(-) with ↑ MN GSTT1(-) + GSTT1(-) with ↑ MN</td>
<td>Cheng et al. (2013)</td>
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<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Genetic damage</td>
<td>Healthy individuals</td>
<td>SCGE, CBMN, CA</td>
<td>GSTT1 (-) with ↑ MN and CA</td>
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<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Genetic damage</td>
<td>Occupational exposure</td>
<td>CBMN</td>
<td>No association</td>
<td>Dusinska et al. (2012)</td>
</tr>
<tr>
<td>GSTP1</td>
<td>Genetic damage</td>
<td>Automobile workers</td>
<td>SCGE, MN</td>
<td>No association</td>
<td>Eshkoor et al. (2011)</td>
</tr>
<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Genetic damage</td>
<td>Pesticide occupational exposure</td>
<td>SCGE</td>
<td>GSTM1(-) with ↑ Tail moment GSTP1(Ile/Ile) with ↑ Tail moment</td>
<td>Singh et al. (2011)</td>
</tr>
<tr>
<td>GSTM1, GSTT1</td>
<td>Chromosomal damage</td>
<td>Road construction workers</td>
<td>CBMN, SCE, HFC</td>
<td>GSTT1 (-) with ↑ MN, sister chromatid exchange and per cent HFC</td>
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<td>GSTM1, GSTT1</td>
<td>Chromosomal damage</td>
<td>Recycling e-waste exposed individuals and healthy controls</td>
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<td>GSTT1 (-) with ↑ MN (exposed group)</td>
<td>Chen et al. (2010)</td>
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<tr>
<td>GSTM1, GSTT1</td>
<td>Genetic damage</td>
<td>Pesticide exposed workers and healthy controls</td>
<td>SCGE</td>
<td>GSTT1(-) with ↑Per cent tail DNA and Damage index, GSTT1(-) + GSTM1(-) with ↑ Per cent tail DNA, DI, DF</td>
<td>Abhishek et al. (2010)</td>
</tr>
<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Chromosomal damage</td>
<td>Occupational exposure and healthy controls</td>
<td>CA</td>
<td>GSTM1 (-) and GSTT1 (-) with ↑ MN frequency</td>
<td>Musak et al. (2009)</td>
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<tr>
<td>GSTM1, GSTT1</td>
<td>Genetic damage</td>
<td>Hemodialysis Patients</td>
<td>8-OHdG</td>
<td>GSTM1(-)↑ level of 8-OHdG</td>
<td>Lin et al. (2009)</td>
</tr>
<tr>
<td>GSTM1, GSTT1</td>
<td>Genetic damage</td>
<td>Genetic damage Pesticide exposure</td>
<td>SCGE, MN</td>
<td>No association</td>
<td>da Silva et al. (2008)</td>
</tr>
<tr>
<td>GSTM1</td>
<td>Genetic damage</td>
<td>Road tunnel construction workers</td>
<td>SCGE, SCE, MN</td>
<td>No association</td>
<td>Villarini et al. (2008)</td>
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<tr>
<td>GSTM1, GSTT1</td>
<td>Genetic damage</td>
<td>CAD patients</td>
<td>MN</td>
<td>GSTT1(+) ↑ MN frequency</td>
<td>Murgia et al. (2007)</td>
</tr>
<tr>
<td>GSTP1</td>
<td>Genetic damage</td>
<td>Farmers exposed to pesticides</td>
<td>SCGE</td>
<td>GSTP1 (wild) with ↑ damage in fruit growers and also significant interaction observed</td>
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</tr>
<tr>
<td>GSTM1, GSTT1</td>
<td>Chromosomal damage</td>
<td>Pooled data from seven laboratories</td>
<td>CBMN</td>
<td>GSTT1 present with ↑ MN frequency</td>
<td>Kirsch-Volder et al. (2006)</td>
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<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Genetic damage</td>
<td>Styrene exposed workers and non-exposed controls</td>
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<td>GSTM1(+), GSTT1(-) and GSTP1 variant with ↑ damage</td>
<td>Buschini et al. (2003)</td>
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<tr>
<td>GSTM1, GSTT1</td>
<td>Genetic damage</td>
<td>CAD patients</td>
<td>MN</td>
<td>GSTM1 null and GSTT1 null with ↑ MN frequency (Smoker CAD patients)</td>
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<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Genetic damage</td>
<td>Coke-oven workers</td>
<td>DNA-adducts</td>
<td>No association</td>
<td>Teixeira et al. (2002)</td>
</tr>
<tr>
<td>Gene</td>
<td>Type of Marker Genetic Damage/Oxidative Stress</td>
<td>Study Group</td>
<td>Assay performed</td>
<td>Outcome</td>
<td>Reference</td>
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<tr>
<td>GSTM1,GSTP1</td>
<td>Genetic damage</td>
<td>Active smokers</td>
<td>DNA-adducts</td>
<td>No association</td>
<td>Piipari et al. (2002)</td>
</tr>
<tr>
<td>GSTM1, GSTT1, GSTP1</td>
<td>Genetic damage</td>
<td>Occupational exposure</td>
<td>HPLC (8-oxodG), SCGE</td>
<td>No association</td>
<td>Marczynski et al. (2002)</td>
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<tr>
<td>GSTM1, GSTT1</td>
<td>Genetic damage</td>
<td>BD exposed workers and controls</td>
<td>DNA adducts</td>
<td>GSTM1 null with ↑ PAH-DNA adducts, GSTM1 null+GSTT1 present with ↑ PAH-DNA adducts</td>
<td>Zhao et al. (2001)</td>
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<tr>
<td>GSTM1</td>
<td>Genetic damage</td>
<td>Women with breast tumor, non-tumor and benign controls</td>
<td>PAH-DNA adducts</td>
<td>GSTM1 null with ↑ PAH-DNA adducts in malignant and non-malignant breast tissues</td>
<td>Rundle et al. (2000)</td>
</tr>
<tr>
<td>GSTM1</td>
<td>Genetic damage</td>
<td>Healthy turkey population</td>
<td></td>
<td>No association</td>
<td>Kocabas et al. (2000)</td>
</tr>
<tr>
<td>GSTT1, GSTM1</td>
<td>Oxidative stress</td>
<td>End stage renal disease patients</td>
<td>MDA, GST levels</td>
<td>GSTT1(-) ↑MDA, GSTM1(-) ↑MDA, GSTT1(-) + GSTT1(+) ↑MDA</td>
<td>EL-Said et al., (2013)</td>
</tr>
<tr>
<td>GSTM1</td>
<td>Oxidative stress</td>
<td>HIV-infected and HIV/HCV co-infected adults</td>
<td>8-oxo-dG, MDA, oxidized glutathione</td>
<td>GSTM1 with ↑ 8-oxo-dG and MDA</td>
<td>Parsons et al., 2013</td>
</tr>
<tr>
<td>MnSOD, CAT, GPX-1</td>
<td>Oxidative stress</td>
<td>Healthy premenopausal women</td>
<td>LC–MS/MS for 8-iso PGF2α &amp; 8-oxo-dG</td>
<td>No association</td>
<td>Al-Alem et al. (2012)</td>
</tr>
<tr>
<td>GSTP1</td>
<td>Oxidative stress</td>
<td>Oesophageal cancer patients and healthy controls</td>
<td>8-oxo-7, 8-dihydro-2'-deoxyguanosine (HPLC)</td>
<td>GSTP1 variant showed positive correlation with 8-oxoG levels</td>
<td>Lagadu et al. (2010)</td>
</tr>
<tr>
<td>GSTM1, GSTT1</td>
<td>Oxidative stress</td>
<td>Diabetic nephropathy patients</td>
<td>GSH, GST and MDA</td>
<td>Combined GSTT1 (-) and GSTM1 (-) genotype ↑ MDA and ↓ GST activity</td>
<td>Ueno et al. (2009)</td>
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<tr>
<td>GSTP1</td>
<td>Oxidative stress</td>
<td>CAD patients</td>
<td>MDA, LDL-C and soluble CD-40</td>
<td>GSTT1 (+) showed ↑ MDA and LDL-C levels</td>
<td></td>
</tr>
<tr>
<td>SOD2</td>
<td>Oxidative stress</td>
<td>Breast Cancer patients</td>
<td></td>
<td>No association</td>
<td>Ahn et al., (2006)</td>
</tr>
</tbody>
</table>

GSTT1 - Glutathione S-transferase theta1, GSTM1- Glutathione S-transferase mu1, GSTP1-Glutathione S-transferase pi 1, SOD2- Manganese superoxide dismutase, CAT- Catalase, GPx- Glutathione peroxidase, SCGE- Single cell gel electrophoresis assay, CA- Chromosomal aberrations, CBMN- Cytokinesis block micronucleus assay, SCE- Sister chromatid exchange
2.7 GST and SODs Genetic Polymorphisms, Genetic Damage and Sports Activity

In sports persons, genetic damage and its modulation by the different GST and SOD2 genotypes has only been studied by one group (Akimoto et al., 2010). Vilela et al. (2010) have studied this in a healthy population. These two studies are reviewed here; the latter because a younger, normal healthy population is included in the age-range of which falls in healthy controls of the present study.

Miranda-Vilela et al. (2010) investigated the influence of haptoglobin, manganese superoxide dismutase (MnSOD Val9Ala), catalase (CAT-21A/T), glutathione peroxidase (GPxPro198Leu), angiotensin-converting enzyme (ACE I/D) and glutathione-S-transferase (GSTT1 and GSTM1) gene polymorphisms on DNA damage and oxidative stress induced by H₂O₂ in vitro exposures in peripheral blood leucocytes of 135 healthy individuals. Significant differences were observed between the age groups of 17-19 and 41-56 year olds (p=0.0021) and 20-40 and 41-56 year olds (p=0.036), and between GPx-1 genotypes Pro/Pro and Pro/Leu (p=0.012) for both moderate and elevated damages after treatment with H₂O₂ at 250 µM. An interaction of GPx-1/ACE polymorphisms (GPx-1 Pro/Leu and ACE DD genotypes) significantly affected genetic damage (treated with 250 µM of H₂O₂, p=0.027) and of Hp1F-1S/M1+T1- on genetic damage (1 mM of H₂O₂ treated, p=0.041). Least damage was observed in GPx-1 Pro/Pro and ACE DD genotypes, and in subjects carrying Hp1F71S/GSTM1+T1+. Haptoglobin (Hp1F71F) genotype was protective against oxidative DNA damage induced by H₂O₂, as treated groups were not significantly different when compared to controls. Hence, GPx-1/ACE and Hp/GSTM1 T1 polymorphisms and interactions can be deterministic for genetic damage and provide higher susceptibility to or protection against oxidative stress-caused damage in healthy persons.

In trained runners (n=135 with at least 4 km run performance), Akimoto et al. (2010) reported that haptoglobin (Hp), MnSOD (Val9Ala), and glutathione-S-transferases M1 (GSTM1) and T1 (GSTT1) genotypes showed deviation from Hardy-Weinberg equilibrium, though CAT, GPx and ACE genotypes were in equilibrium. There were significant differences between genders for aspartate amino transferase (AST) and creatine kinase (CK) levels being higher in males while DNA damage (comet assay)
was higher in females. There was a significant influence of MnSOD polymorphism for CK values with Ala/Ala genotype having least CK value compared to Val/Val (p=0.013) and Val/Ala (p=0.025) genotypes. Haptoglobin sub-types also influenced the results of TBARS assay (p=0.051), with marked differences between Hp1F-1S and Hp1S-1S (p=0.006), and between Hp1S-1S and Hp1S-2 (p=0.003) genotypes. An interaction between Hp/GSTM1 and Hp/GSTT1 was significant for CK (p=0.005 and p=0.007, respectively). Genetic damage was highest in Hp1F-1S and GSTM1+T1+ genotyped individuals and least damage in Hp1F-1F/GSTM1+T1+ genotypes. For comet assay, a significant interaction of Hp1F-2/ACE DD and II (p=0.048) caused greatest damage with least damage in 1F1F/ACE genotypes. The authors highlighted that MnSOD and Hp polymorphisms could be deterministic of performance in runners.

Against the backdrop of literature reviewed here, the present study was planned with the aim to investigate DNA and oxidative DNA damage in blood samples of some players and to find if the genetic damage was modulated by some genotypes. In the literature, similar studies on sports persons from this part of the region have not come to attention. The genetic damage assays and oxidative stress biomarkers used for the objectives of the present study are well-validated. The selected genetic polymorphisms have not been extensively studied for modulation of genetic damage in sportspersons. Hence the present study was purposed to fill these knowledge lacunae.