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Genetic variants and flexibility in relation to non-contact injury risk among young basketball players

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ABSTRACT

This study aimed to compare the injury status of juvenile basketball players based on their genetic variants and flexibility capacities. Conducted between October 2019 and February 2020, the cross-sectional study included 17 U-15 professional male basketball players from the same team, who participated voluntarily. Genotypes of GDF-5 rs143383 and IL-6R rs2228145 SNPs were identified. Flexibility was measured (sit and reach) at two time points (BS, MS). Non-contact injuries recorded by team physicians were compared among genotypes. Due to the limited sample size, findings should be considered exploratory. The GDF-5 TT genotype showed a significantly higher injury incidence compared to CC (p=.011). IL-6R AC carriers showed higher flexibility values but without statistically significant differences in injury frequency (p>.05). These preliminary findings suggest GDF-5 TT may confer elevated injury risk. Given the limited statistical power, further research with larger cohorts is necessary.

KEYWORDS

Injury; Flexibility Capacity; Genetic; Young Basketball Players

1. INTRODUCTION

Maintaining current performance by averting injuries is a crucial success factor for any team or individual athlete. However, injuries to athletes occurring during sports activity is a frequent occurrence. Every physical activity has its own incidence of injury, whether they are competitive sports or recreational activities for enjoyment and good health. In basketball, which is one of these competitive physical activities; especially among young basketball players, the frequency of applying

to emergency services of hospitals with the complaint of injury after training/competition is very common (Harmer, 2005). Due to abrupt shifts in direction and forceful landings after leaping, knee and foot injuries are the most prevalent in basketball. While ankle injury (35.9%) and knee injury (5-20%) are in the first two ranks, head traumas, injuries to teeth, shoulders and fingers are the most common ones (Malloy et al., 2015). It has been observed that most basketball injuries happen during games against the other team, not during practise at school or in sports clubs (Arnold et al., 2017; Malloy et al., 2015). The causes of injuries are complex mashups of external and internal factors. The primary risk factors for injuries in the basketball branch are rapid development phases, exercise intensity, chronological age, prior injuries (Arnold et al., 2017), flexibility ability (Herbert & Gabriel, 2002), improper and inadequate warming up (McCrary et al., 2015), and genetic factors (Hashimoto et al., 2008; Lulińska-Kuklik et al., 2019; Smith et al., 2012). On the other hand, warming-cooling and static-dynamic stretching exercises are one of the methods used to increase and maintain the range of motion of the muscles and joints in order to prevent injuries. For many years, static flexibility in sports injuries has been debated as a method of injury avoidance in numerous scholarly papers (Herbert & Gabriel, 2002; Gleim & McHugh, 1997; Miyamoto-Mikami et al., 2019; Kıratlı & Sanioğlu, 2005). Flexibility is one of the common characteristics of the muscles. Flexibility is recognised as a motor skill that provides body mobility through the range of motion in a joint or succession of joints (Fox & Methews, 1974). It has been reported that sufficient flexibility for joint mobility may be the best protection for muscle and connective tissue injuries (Sporis et al., 2011).

Recent genetic research continues to identify specific markers linked to athletic injuries and performance. The total number of DNA polymorphisms associated with athlete status was reported to be 220 by the end of 2020 (Ahmetov et al., 2022). On the other hand, 124 SNPs have been identified that are associated with athlete health and injury (bone mineral density, osteoarthritis, vitamin and mineral deficiencies, stress fracture, ACL rupture, Achilles tendon injury, and sickle cell trait) (Goodlin et al., 2015). Genome-wide association studies (GWAS), which relate genetic structures to health and disease, continue to introduce to the field of sports science single-nucleotide polymorphisms (SNPs) with genome-wide significance in relation to sports performance and athletic health.

In light of this information, we determined the GDF-5 rs 143383 and IL-6R rs 2228145 SNPs after a large literature review to compare the injuries sustained by elite young basketball players to their genetic structures.

From these SNPs (GDF-5) growth and differentiation factor 5 gene; encodes the growth differentiation factor 5 protein, which is known to influence the growth and maintenance of bones, muscles, and tendons. This gene's rs143383 SNP contains three different variants, CC, CT, and TT. Members with the T allele produce less GDF5 protein and have been associated with the occurrence of joint calcification and other disorders (Goodlin et al., 2015). The GDF5 gene has been associated with strength performance, stress fractures, and muscle regeneration in previous research (Hatazawa et al., 2018; Zhao et al., 2016).

Interleukin 6 receptor (IL 6) encodes IL-6R as a subunit of the receptor complex. Interleukin 6 is a potent pleiotropic cytokine that regulate cell growth and differentiation and plays a crucial role in the immune response (Hoek et al., 2008). The single nucleotide polymorphism (SNP) rs2228145 in the IL-6R locus results in the replacement of Aspartic acid for Alanine at codon 358. This change in the major Asp358 variant (A allele) and minor Ala358 variant (C allele) was found to cause a roughly twofold increase in the plasma concentration of sIL-6R in the CC genotype compared to the AA variant (Rafiq et al., 2007). This SNP has been linked to a variety of conditions, including rheumatoid arthritis (Ahmed et al., 2017; Nishimoto, 2006), ACL rupture (Lulińska-Kuklik et al., 2019), and concussion risk (Terrell et al., 2018), according to previous research. Newly, people with the rs2228145 AA genotype have been found to have greater activity levels, whereas those with the classic trans-C variant have higher sIL-6R signal levels. Because of this, it has been reported that the CC genotype causes increased trans-signalling and (reduced classical signalling) after exercise, which lowers exercise endurance and self-selected physical activity levels (Webb et al., 2021).

Research investigating genetic indicators for sports injuries typically focus on cohort and control groups, which are made up of players from various sports. However, for our research, we chose 17 basketball players from the national U-15 basketball league's Galatasaray U-15 young team. The first cause for this is that Galatasaray sports club is one of the most established professional sports teams in Turkey's basketball league. All of the athletes had at least 5 years of professional training experience, got fitness and camp preparatory training each season, and had 6 training sessions and 1 match experience per week. Second, we wanted to see the results under the same exercise protocols and the same conditions within a single team. This is because many factors, such as the criteria for choosing an athlete for a team in different branches and teams, training, diet, success expectations, and ranking in the league, will be different and will affect the likelihood that an athlete will get hurt.

The aim of this study is to investigate the interaction between hereditary traits and flexibility capacities in relation to non-contact injuries among young basketball players. We hypothesized that the GDF-5 rs143383 TT genotype previously reported in the literature as a risk allele and the IL-6R rs2228145 genotypes known for their cytokine effects on joint and cartilage structures, particularly in rheumatoid arthritis might be associated with non-contact injury status within our study's limited sample size.

2. METHODS

2.1. Participants

A post hoc power analysis was conducted using G*Power (version 3.1) with an assumed medium-to-large effect size ($f = 0.40$), $\alpha = .05$, and desired power ($1-\beta$) = 0.80 for a one-way ANOVA comparing three genotype groups. The analysis indicated that a minimum total sample size of approximately 63 participants would be required to detect statistically significant differences. Given that this study included only 17 athletes, the findings should be interpreted with caution and considered exploratory in nature.

It was made up of 17 male players that volunteered from the Turkish U-15 Men's Basketball League's Galatasaray Sports Club. All of the athletes had at least five years of professional training experience, got preseason conditioning and camp training each year, and participated in 6 training sessions and 1 match each week. The research was done in compliance with the ethical principles of the Declaration of Helsinki and with the approval of the local university's Ethics Committee (61351342/2020-478). The participants' parents and team coordinator gave their approval, and the information and consent form were signed.

2.2. Experimental Design

This cross-sectional study was conducted between October 2019 and February 2020. Data collection took place in 2 stages (BS: Beginning Season start and MS: Mid-season). Genetics expert Dr. gathered mouth swab samples from participants at the beginning of the season. As season start (BS) test data, the height, weight, and flexibility capacities (sit and reach) of the athletes were measured and recorded. MS: During the middle of the season, anthropometric measurements and flexibility capability tests were redone. Throughout the season, all athletes' injuries were documented by the team physician and physiotherapist. All measurements were took place between the same hours (11:00 and 13:00) at 21^0C and 52–55 percent humidity on the basketball floor of the Galatasaray Sports Club. UNI-T UT333 was used to measure the temperature and humidity (Hong

Kong). Training regimens in which athletes were in a resting condition for at least 48 hours were taken into account in order to avoid being impacted by performance variability brought on by delayed muscle discomfort. All players were familiar with tests and experimental procedures.

2.3. Genetic Sampling and Variation Analysis

A swab stick was used to collect oral culture for DNA analysis. This procedure was carried out by a genetics expert doctor, and the samples were sent to the laboratory under special storage conditions. Oral swab samples were genotyped for IL-6R rs 2228145 A>C and PDF-5 rs 143383 C>T. The extraction of genomic DNA from the oral mucosa samples was carried out by automatic extraction in QIACube equipment (QIAGEN, Venlo, Netherlands), with a DNA concentration yield of 25-40ng/ml, which was kept in solution in a volume of 100 microliters at -20^{o}C until genotyped. All the selected genes were genotyped by multiplex analysis by Polymerase Chain Reaction-Single Nucleotide Primer Extension (PCR-SNPE), a multiplex-PCR for amplication of targeted sequences, followed by single-base extension assay of probe-primers using the commercial SNaPshot Kit (Applied Biosystems, Foster City, CA) in the Real Time-PCR instrument QuantStudio5 (QS5) (Thermosher, CA).

2.4. Anthropometric Measurements

Age determination; The athletes' identities were established based on their birth dates. Height was measured using a 0.1 cm sensitivity (Holtaine, England) stadiometer. With the Tanita BC 418 (Japan) body analyzer, the body weights of the athletes were measured by wearing only shorts.

Flexibility Measurement (Sit and reach test): Before the test of flexibility, the athletes performed a general warm-up to increase their heart rate, blood flow, body temperature, and respiration. It included 5 minutes of running and joint-specific dynamic and static stretching routines. We employed the sit and reach test, whose validity and reliability were established in the basketball branch by Sporis et al., (2011) to assess the players' flexibility potential. Athletes sat with their legs parallel to the floor and their bare feet (shoes off) contacting the measurement table. The upper torso was at a 90-degree angle to the ground, the arms were stretched forward, and the measuring tape was zeroed out. Without moving the knees from the ground, with the hands-on top of each other and the palms facing down, the measuring ruler was pushed to its farthest point by bending forward, and 2 seconds were spent in this posture. The test was administered twice, and the highest score was considered.

2.5. Statistical Analyses

Means, standard deviations, frequencies and percentages were used to define the age, height and body weight, dominant foot and arm characteristics of the athletes. The Shapiro-Wilk test was used to see if the genotypes' injury and flexibility data were normally distributed. The injury data were not normally distributed ($p<.05$) Kruskal-Wallis (Bonferroni correction multiple tests) was used to assess the non-parametric flexibility and injury value averages. Data were expressed as mean±standard deviation, with significance set at $p<.05$. All statistical analyses were performed using IBM SPSS Statistics version 28 software for Windows (IBM Corp., Armonk, NY, USA) software.

3. RESULTS

The mean age (14.82 ± 0.39 years), height (192.18 ± 6.33 cm), and body weight (79.17 ± 7.62 kg) of the 17 youth basketball players who participated in the study were recorded. Table 1 presents the allelic distribution of the GDF-5 rs143383 and IL-6R rs2228145 genotypes, along with the number of injured athletes and the corresponding injury frequencies.

Table 1. Distribution of GDF-5 rs143383 and IL-6R rs2228145 genotypes among youth basketball players, summarizing the number of athletes, injury frequency, and injury rate (%)

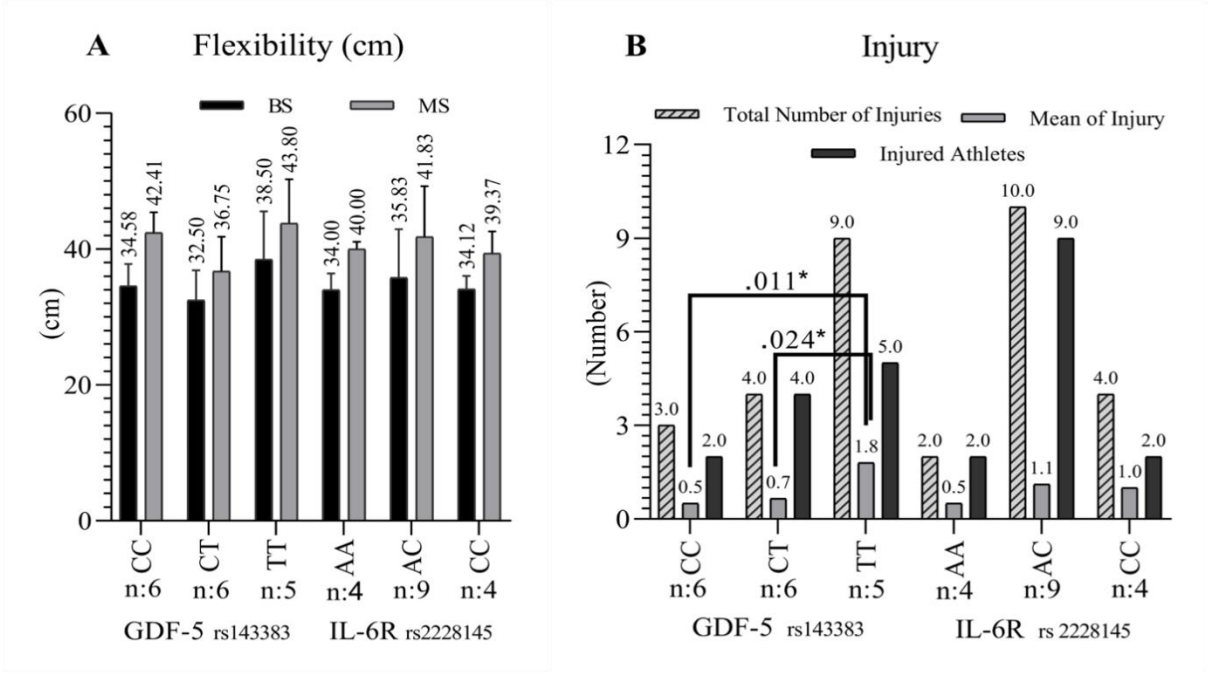
Genotype	n	Injury Frequency	Injured Athletes (n)	Injury Rate (%)
GDF-5 CC	6	2	2	33.3
GDF-5 CT	6	4	4	66.6
GDF-5 TT	5	9	5	100
IL-6R AA	4	2	2	50
IL-6R AC	9	10	7	77.7
IL-6R CC	4	2	2	50

Table 1 shows that injury rates varied across genotypes. For GDF-5 rs143383, the injury rate increased from 33.3% in CC to 66.6% in CT and 100% in TT. For IL-6R rs2228145, the highest injury rate was observed in the AC genotype (77.7%), compared with 50% in both AA and CC. Table 2 below shows the Kruskal–Wallis comparisons of injury outcomes between different genotypes, while Figure 1 shows flexibility performance and injury averages across GDF-5 and IL-6R genotypes at the beginning and middle of the season.

Table 2. Kruskal-Wallis test results for genotype comparisons with effect sizes (η^2)

Comparison	H Statistic	p-value	Sample Size (n)	η^2 (Effect Size)
GDF-5 TT vs CC	5.90	0.015	11	0.544
GDF-5 CT vs CC	2.40	0.121	12	0.140
IL-6R AC vs AA	3.10	0.078	13	0.191
IL-6R AC vs CC	1.80	0.178	13	0.073

Note. *η^2 values were calculated using the formula $\eta^2 = (H - k + 1) / (n - k)$, where H is the Kruskal-Wallis test statistic, k is the number of groups, and n is the total sample size for each comparison.*



Note. * p<.05 BS: *Early season* ***MS:*** *Mid-season*

Figure 1. Comparison of GDF-5 rs143383, IL-6R rs2228145 genotypes' flexibility performances at the beginning and middle of the season and their injury averages during the season

There was no significant difference between GDF-5 and IL-6R genotypes in terms of flexibility capacity (p>.05). The TT genotype of GDF-5 had a higher average injury rate during the season than both CC (p=.011) and CT (p=.024) genotypes. Athletes with GDF-5 TT genotype had the highest flexibility performance (BS:38.50±7.05, MS:43.80±6.46 cm, respectively). The average injury rates of IL-6R genotypes during the season did not differ significantly (p>.05). Quantitatively, IL-6R AC genotype AA had the highest mean injury rate (1.1+0.78) and the highest flexibility performance (BS:35.83±7.10, MS:41.83±7.45 cm) compared to CC.

4. DISCUSSION

The primary finding of this exploratory study was that the GDF-5 rs143383 TT and IL-6R rs2228145 AC genotypes were associated with the highest frequency of non-contact injuries among youth basketball players trained under uniform conditions within a single team. Although no statistically significant differences were observed in flexibility performance across genotypes, the TT and AC carriers—who also exhibited the highest injury frequencies—had quantitatively superior flexibility values.

Comparative analyses of flexibility and injury revealed that athletes with the GDF-5 TT genotype sustained a total of nine injuries, with all five TT carriers experiencing at least one injury. This resulted in a 100% injury rate among this subgroup. In contrast, the CC genotype was associated with the lowest injury incidence, with only two of six athletes sustaining injuries (33.3%). The difference between TT and CC genotypes was statistically significant ($p = .049$). The CT genotype represented an intermediate risk profile.

Regarding IL-6R, the AC genotype showed the highest injury frequency (10 injuries among 9 athletes; 77.7%), followed by the AA and CC genotypes (both at 50%). Notably, three injured athletes who were AC carriers also possessed the GDF-5 TT genotype, suggesting a potential additive effect; however, due to the small sample size, this interpretation remains speculative.

Overall, 16 non-contact musculoskeletal injuries were recorded, including spondylolysis (4), ACL injuries (3), ankle sprains (3), stress fractures (3), patellar tendinitis (1), groin injury (1), and one case of shoulder impingement. Despite higher average flexibility values, TT and AC genotypes were not protected from injury, indicating that static flexibility alone may not serve as a preventive factor for non-contact injuries in adolescent basketball players. This aligns with earlier findings suggesting that greater flexibility does not universally translate to reduced injury risk (Miyamoto-Mikami et al., 2019; Kıratlı & Sanioğlu, 2005).

The GDF-5 gene, known to regulate musculoskeletal tissue growth and maintenance, has previously been associated with stress fractures, joint degeneration, and ligament injuries (Goodlin et al., 2015; Hatazawa et al., 2018). Our finding of higher injury incidence among TT carriers is consistent with reports identifying the T allele as a risk factor for joint-related injuries (Harsanyi et al., 2021; Zhang et al., 2015).

For IL-6R rs2228145, the results were less conclusive. Although previous studies identified associations between IL-6 signaling variants and inflammation or ACL injuries (Hashimoto et al.,

2008; Terrell et al., 2018), the role of the AC genotype in injury predisposition remains uncertain and was not statistically significant in our cohort.

Importantly, our study has several limitations. The sample size was small, which severely limits statistical power and the ability to control for confounding variables such as previous injury history, biological maturation, training load, or biomechanical asymmetries. Injury incidence was not standardized by exposure time (e.g., per 1000 player-hours), which precludes direct comparison with established injury epidemiology in sports science literature.

Nevertheless, these preliminary findings suggest that specific genetic variants may contribute to injury susceptibility profiles in young athletes. However, they should not be interpreted as definitive without replication in larger, well-controlled studies.

5. CONCLUSIONS

Our results suggest a potential association between GDF-5 TT genotype and higher injury risk among young basketball players. Although IL-6R AC genotype showed higher flexibility levels, injury associations were not statistically significant. The limited sample size restricts broader conclusions. Future studies with larger samples and controlled confounding variables are needed to validate these preliminary findings.

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All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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