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Research Article

ANALYSIS OF P AND Q ARMS OF CHROMOSOMES AND ITS EFFECTS ON THE CAUSES OF SCOLIOSIS DISORDERS

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ABSTRACT

The spine is very delicate structure of the human body. The spinal cord is located inside the spine. Vertebrae are small bone forming the spinal column. Human spine has natural "S" curve. These curves round our shoulders and make our lower back curve slightly inward. Spine has three slight curves one in the neck, one in the upper back, and another in the lower back. These curves are normal and can be seen from a side view. From a back view, spine should appear straight. If a spine have side to side curve the curve is called scoliosis. The curve may be very small (mild). It may be bigger (moderate). Or it may be sharp (sever). Scoliosis is present in 0.2 – 6% of the population, affecting females in most cases. Scoliosis affects Young girls engaged in rhythmic gymnastics, swimmers, professional musicians and dancers. The gathering of all the genetic data on spinal cord disorders, then a comparative analysis was performed on the various types of genes and their biological factors which are the likely to cause scoliosis in either mutant or deficiency forms. The q-arm contributes to scoliosis disorder than the p-arm. Scoliosis is prevalence among most active group between 18-70 years.

INTRODUCTION

The spine is a column of small bones, or vertebrae, that support the entire upper body. The column is grouped into three sections of vertebrae: The cervical (C) vertebrae are the five spinal bones that support the neck. The thoracic (T) vertebrae are the twelve spinal bones that connect to the rib cage. The lumbar (L) vertebrae are the five lowest and largest bones of the spinal column. Most of the body's weight and stress falls on the lumbar vertebrae. Below the lumbar region is the sacrum, a shield-shaped bony structure that connects with the pelvis at the sacroiliac joints. At the end of the sacrum are two to four tiny, partially fused vertebrae known as the coccyx or "tail bone. Spine has three slight curves one in the neck, one in the upper back, and another in the lower back. These curves are normal and can be seen from a side view. From a back view, your spine should appear straight. If a spine have side to side curve the curve is called scoliosis. The curve may be very small (mild). It may be bigger (moderate). Or it may be sharp (sever). Spine has three slight curves one in the neck, one in the upper back, and another in the lower back. These curves are normal and can be seen from a side view. From a back view, your spine should appear straight. The vertebras of the lower back are connected by ligaments which attach bone to bone, and tendons that connect muscle to bone. The main lower back muscles maintain the arch in the spine known as the lordotic curve, while the upper back maintain a reverse curve known as kyphosis. These curves can be changed by injuries and weakening of these muscles. When the lower back and upper back lose its normal curves, injury and back bone pain become an increasing risk. Ligaments and muscles of the back may be injured through a traumatic tearing of the fibers known as a sprain (ligament tearing) and strain (muscle tearing). The spine is very delicate structure of the human body. The spinal cord is located inside the spine. Vertebrae are small bone forming the spinal column. Human spine has natural "S" curve. These curves round our shoulders and make our lower back curve slightly inward. In poor posture, the spine will be bent on sides. Kyphosis is a curve seen from the side in which the spine is bent forward. Lordosis is a curve seen from the side in which the spine is bent backward. People with scoliosis develop additional curves to either side, or the bones of the spine twist on each other like a corkscrew. These curves can't be corrected simply by trying to stand up straight. Scoliosis is a disorder that

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causes an abnormal curve of the spine, or backbone. The spine has normal curves when looking from the side, but it should appear straight when looking from the front. Scoliosis is about two times more common in girls than boys. It can be seen at any age, but it is most common in those over 10 years old. However, there is no correlation between the severities of the curves between the age groups. In most cases, the cause of scoliosis is unknown (idiopathic). This type of scoliosis is described based on the age when scoliosis develops. If the person is less than 3 years old, it is called infantile idiopathic scoliosis. Scoliosis that develops between 3 and 10 years of age is called juvenile idiopathic scoliosis, and people that are over 10 years old have adolescent idiopathic scoliosis (Gummerson *et al*, 2011). Scoliosis is present in 0.2 – 6% of the population, affecting females in most cases (Wilson, 2013).

Young girls engaged in rhythmic gymnastics (Micheli 1983; Cirillo, and Jackson, 1985; Sward *et al*., 1990) had a 10-fold increased risk for scoliosis. Scoliosis if not detected and checked earlier can affect the performance of swimmers (Becker, 1986), athletes (Green *et al*., 2008; Stosic *et al*., 2011), professional musicians and dancers (Bird and Pinto, 2013; Steinberg *et al*., 2013).

Gene Abnormalities for Adolescent Idiopathic Scoliosis (AIS)

Many abnormalities associated with this condition have been described, and the debate on whether Idiopathic Scoliosis **(**IS) is a primary or secondary disorder is still open. These abnormalities include disorders of the central and the peripheral nervous system maturation (such as the vestibular system affecting proprioception), of the connective tissues (such as elastic and collagen fibers found in ligaments), muscles and bones. Other related diseases include platelet disorders and several molecular biology anomalies (such as melatonin, calmodulin, and growth hormones levels). For many of these disorders, specific gene abnormalities were described. Adolescent idiopathic scoliosis (AIS) is considered an inherited complex disease of childhood. Genetic twin studies and observation of familial aggregation revealed significant genetic contribution to IS. Familial forms of IS (FIS) were described as early as 1922. There are now many well-recognized skeletal deformities in man which are inherited according to Mendelian law, and a large proportion of these are inherited as Mendelian dominants-that is, each affected person has an affected parent and an affected grandparent, and on the average half the children of an affected parent are themselves affected; among the commoner skeletal defects inherited in this way is brachydactyly. One of the commonest deformities seen in hospital practice is scoliosis, the causes of which are numerous and often clearly understood, but there seems to be considerable doubt as to the importance played by heredity in the production of this condition **(Hugh, 1934)**. Since then, reports of multiple twin series have shown higher concordance in monozygotic compared to dizygotic twins. Autosomal dominant inheritance of infantile IS has been suggested from evaluation of single families or small family collections. A genetic survey study reported an overall risk of IS to first-degree relatives of 11% compared to 2.4 and 1.4% in more frequently encountered in females than in males. **Cowell *et al.* (1970)** reported that the second- and third-degree relatives, respectively, suggesting inheritance is multi factorial. IS is possibility that Idiopathic Scoliosis may be determined on genetic basis has not been considered in the past by orthopedic surgeons in the past. The evaluations and testing more than 1400 patients with Idiopathic Scoliosis lead the author and his team to believe that Idiopathic Scoliosis is an inherited condition. **Kimberly (1997)** compared and contrasted the concordance, severity, and curve patterns in monozygotic and dizygotic, twins with adolescent idiopathic scoliosis in an attempt to document a genetic etiology and delineate inheritance patterns for adolescent idiopathic scoliosis.

He discovered that Monozygous twins have a significant higher rate of concordance than dizygous twins and the curves in monozygous twins, develop and progress together. Based on these data, there is strong evidence for a genetic etiology for adolescent idiopathic scoliosis. **Justice *et al.* (2006)** studied 1,198 patients from 202 families who had at least two individuals with IS. Their results indicated that 15% of these families presented a locus on the X chromosome that could be linked to familial idiopathic scoliosis, suggesting an X-linked dominant mode of inheritance in some patients. **Montanaro *et al.*** 2006 showed evidence of a linkage between idiopathic scoliosis and three microsatellite polymorphisms in the *MATN1* gene (encoding for Matrilin 1, cartilage matrix protein), respectively consisting of 103, 101 and 99 base pairs. Autosomal dominant inheritance has been suggested from evaluation of single families or small family collections. X-linked dominant inheritance has been a prevailing theory to explain apparent lack of male-male transmission. However this was disputed after re-evaluation of X-ray data from original study subjects. **Wise *et al.* (2007)** reported that at least one gene, CHD7, has been associated with the idiopathic form of scoliosis. Studies conducted by Various studies have found that IS disease risk falls off quickly comparing first-degree relatives of a pro-band to subsequent generations **(Xiaochong *et al.*, 2008).** These observations may be most consistent with a multi-factorial inheritance model involving many genes, interplaying with unknown environmental factors. The general consensus gathered from all of this is that, while families with dominant inheritance may exist, IS is generally a "complex" genetic disease that is not easily explained by existing inheritance models. Other molecular studies found that isolated critical regions on autosomal chromosomes also had potential importance in the occurrence of scoliosis. Candidate regions on chromosomes 6, 9, 16, and 17 were considered to have the strongest evidence for linkage a cross all subsets of scoliosis-families studied **(Romaine *et al.*, 2013).**

The Role of Heritable Genes in the Occurrence and Development of AIS

Heritable and genetic factors have been found to play a vital role in the occurrence and development of AIS. Several loci associated with predisposition to AIS have been identified in genome-wide linkage studies in such regions as 6p, 10q, 18q, 19p13.3, 17p11, 19p13, 8q12, 9q31.2-q34.2, 17q25.3-qtel, 12p, and Xq (Wenjie, 2013). Single nucleotide polymorphisms (SNPs) in the genes for estrogen receptor a (ESR1), estrogen receptor b (ESR2), matrilin 1 (MATN1), melatonin receptor 1B(MTNR1B), tryptophan hydroxylase 1(TPH1), interleukin-6 (IL-6) and matrixmetalloproteinase-3 (MMP-3) have been reported to be associated with AIS predisposition. However, so

far these studies have not been replicated in other ethnic groups. Polymorphisms of ESR1, ESR2, MATN1, insulin-like growth factor-I (IGF-I), tissue inhibitor of metalloproteinase-2 (TIMP-2), G protein-coupled estrogen receptor 1 (GPER), and neurotrophin3 (NTF3) have been reported to be associated with the severity of curvature in AIS. These might be the modifier genes for AIS, but at present there is a lack of conclusive functional studies. Genetic association studies are the means of identifying risk variants in complex traits, and replication studies that confirm their findings in other ethnic groups are quite necessary. A genome-wide association study (GWAS) was performed in a Japanese population, and three SNPs (rs11190870, rs625039 and rs11598564), all of which were located near the gene LBX1 on chromosome 10q24.31 **(Wenjie *et.al*, 2013).**

Degree of the Curvature for Scoliosis Detection

In general, the severity of the scoliosis depends on the degree of the curvature and whether it threatens vital organs, specifically the lungs and heart.

Effect of Mild Scoliosis (less than 20 degrees): Mild scoliosis is not serious and requires no treatment other than monitoring.

Effect of Moderate Scoliosis (between 25 and 70 degrees). It is still not clear whether moderate scoliosis causes significant health problems. In one study **(Kesten *et al.*, 1991)**, adults with moderate scoliosis had normal lung function, although they had difficulty exercising. (The researchers believed that this low exercise tolerance might have been because many patients with scoliosis do not engage in regular physical activity).

Effect of Severe Scoliosis (Over 70 degrees): If the curvature exceeds 70 degrees, the severe twisting of the spine that occurs in structural scoliosis can cause the ribs to press against the lungs, restrict breathing and reduce oxygen levels. One study (Asher and Burton, 2006), concluded that almost two-thirds of patients with curves of 90 degrees and under had less than 80% of normal lung capacity. The distortions can also affect the heart and cause dangerous 7

Effect of Very Severe Scoliosis (Over 100 degrees): Eventually, if the curve reaches over 100 degrees, both the lungs and heart can be injured. Patients with this degree of severity are susceptible to lung infections and pneumonia. Curves greater than 100 degrees increase mortality rate, but this problem is very uncommon **(Asher and Burton, 2006).**

Calculation of the Curve of Spine: The degree of the spinal curve is nearly always calculated using a technique known as the Cobb Method.

On an X-ray of the spine, the examiner draws two lines. One line extends out and up from the edge of the top vertebrae of the curve. The second line extends out and down from the bottom vertebrae. A perpendicular line is then drawn between the two lines. The intersecting angle is measured to determine the degree of curvature.

The Cobb method is limited because it cannot fully determine the three-dimensional aspect of the spine. It is not as effective, then, in defining spinal rotation or kyphosis. It also tends to over-estimate the curve. Other diagnostic tools are needed to make a more accurate diagnosis.

An improved technique using calculations based on geometric principles of the apex of the curve as well as the top and bottom of the curve may prove to be accurate in determining all the dimensions of the curve **(Suken *et al*., 2009).**

Chromosome region for adolescent idiopathic scoliosis (AIS and IS)

Salehi *et al.* (2002) found regions linking adolescent idiopathic scoliosis to chromosome17, through the investigation three generations of a family of Italian origin with 11 members affected, who presented curves between 10 and 20 degrees and autosomal dominant inheritance pattern with complete penetrance. This study located chromosome 17p11 linked to idiopathic scoliosis. **Ocaka *et al.* (2007)** found chromosomal regions in chromosomes 9q34 and 17q25. **Montanaro *et al.* (2006)** conducted a study aimed at investigating the loci responsible for susceptibility to idiopathic scoliosis in a genome-wide linkage survey identified, and a limited number of genetic loci predisposing to idiopathic scoliosis (IS) evidence of allele-sharing in one family was detected for three loci on chromosome 6p, 10q, and 18q. Another study found a linkage with IS at locus 17p11 in a three generation IS Italian family 9 and another linkage with IS was found at locus 19p13.3 in a Chinese family. The results obtained from the analysis of transmissions of the allelic variants of the microsatellite marker internal to matrilin-1(MATN1) gene, in a population of trios composed of children affected by IS and their parents, show the presence of a linkage between the allele and IS. It is actually more correct to talk about susceptibility to scoliosis because the genetic expression of IS may be dependent on multiple factors and genetic interactions. MATN1 gene is mainly expressed in cartilage. Its proteic product, also known with the alternative name of cartilage matrix protein, is an extracellular matrix structural constituent, which is associated with cartilage proteoglycans as well as being a component of both collagen-dependent and collagen-independent fibrils. **Gao *et al.* (2007),** soughted to refine the search for IS susceptibility loci and to identify contributing genes, by following up results of genomewide scans in a new set of multiplex families with IS. All participated research subjects were ascertained under a protocol approved by the University of Texas Southwestern Medical Center Institutional Review Board. The *SNTG1* gene disrupted in the 8q inversion breakpoint was detected, other genes like, chromodomain helicase DNA-binding protein 7 gene (*CHD7)* was also indentified. The reduction of functional CHD7 in the postnatal period, particularly during the adolescent growth spurt, may disrupt normal growth patterns and predispose an individual to spinal deformity. The strongest results was obtained for 8q12 loci . This revealed positive evidence of linkage between IS and chromosome 8q loci in the more proximal region that had provided modest evidence of linkage. The chromosome 8 has been most progress, where CHD7and SNTG1have been proposed as candidate genes. Previous work has also suggested the possibility these genes contribute to AIS. The chromosome region 12 susceptibility loci is gene rich, and have 95 known genes and a similar number of uncharacterized known or potential transcripts. Some of the genes are susceptible for AIS. These include genes encoding ion channels (KCNA1,KCNA5 KCNA6, SCNN1A), bone-derived growth factors (GDF3), growth factors regulating muscle (FGF6), and

neurons (NTF3),enzymes involved in protein processing (USP5, SPSB2), and components of the extracellular matrix (MFAP5) **(Raggio *et al.*, 2009).** Several research studies of AIS says the most progressive chromosome region has been made on chromosome 8, with *CHD7* and *SNTG1* as genes. Previous work has also suggested the possibility that genes' contributing to AIS when mutated is responsible for known genetic syndromes (Cathleen *et al.*, 2009**).** Another study conducted by **Clough *et al.* (2010)**, confirmed, the relationship between the region described by **Salehi *et al.* (2002),** and familial idiopathic scoliosis, when studying 17 families. Genetic factors are thought to contribute to the development of scoliosis, as demonstrated by an increased incidence (6–11%) in first-degree relatives. Previous analyses of several moderate-sized Caucasian families gave some evidence for linkage to three loci on chromosomes 6p, distal 10q, and 18q. An additional locus on chromosome 17p was identified in a large Italian family. However, linkage of scoliosis to these loci has not been replicated. Evidence for linkage to chromosome 19p was demonstrated in one large Chinese family with AIS and confirmed in a separate Caucasian family, but no causative gene mutations have been found. More recently, linkage and association of AIS was demonstrated to single nucleotide polymorphisms on chromosome 8q within CHD7, the gene responsible for CHARGE syndrome, making it the first recognized AIS susceptibility gene **(Gurnette *et al.*, 2010).** In 2011, **Takahashi *et al***. performed an important multi-center study. About 1050 Japanese women with AIS and 1,474 control women without AIS were evaluated using of curves greater than or equal to 15 degrees as the criterion for affected patients, by Using a genome-wide association study (GWAS), it was successfully correlated that the chromosome region 10q24.3 is within the region 10q which contains LBX1 gene was associated with AIS. Other family studies over the years have suggested that AIS is related to chromosomes 6, 9, 16 and 17, and to the chromosomal regions 17p11, 19p13.3, 8q12 , 9q31-q34.2, 17q25.3, and 12, 18q12.1-12.2 **(Wajchenberg *et al.*, 2015). X-linked inheritance of adolescent idiopathic scoliosis (AIS) or Idiopathic scoliosis (IS)**

Male-to-male transmission is apparently rare and was specifically absent in 17 families studied by **Cowell *et al.* (1972**), who suggested X-linked dominant inheritance. The 8 to 1 ratio of females to males supports this conclusion that there is X chromosomal linkage. Report written by the national Institutes of Health, Maryland, USA, says that a region on the X chromosome may be linked to the expression of familial idiopathic scoliosis in families. If the scoliosis genes are located on the X chromosome the means that it will give rise to various disorders. Severe scoliosis is more common in females than males, at a ratio of 4:1.Males only have one X chromosome, whereas females have two **(Justice *et al.*, 2003). Ward *et al.* (2009**) studied 69 extended Utah families with a history of adolescent idiopathic scoliosis, including a total of 247 affected individuals with disease confirmed by x-rays and medical records. He concluded that the condition is polygenic and multifactorial. Excluding all probands and assuming autosomal dominant inheritance, 1,260 individuals over the age of 16 years were determined to be at risk because they had a parent with AIS. This controversy regarding the inheritance pattern of IS served as the rationale to investigate X-linkage as a potential inheritance pattern in familial idiopathic scoliosis (FIS). Through the use of a large sample of families affected with idiopathic scoliosis. Genomic screening and statistical linkage analysis was done. It was previously reported that Xq26 as a susceptibility locus for FIS within a subgroup of FIS families. The current studies support that within a subset of families affected by familial idiopathic scoliosis a genetic determinant on the X-chromosome predisposes individuals to this disorder **(Miller *et al.*, 2010).**

Giampietro (2012) performed study to determine the genetic factors that may predict curve progression in IS females.304 females with IS demonstrated significantly greater Cobb angle at the time of growth maturation among patients with estrogen receptor genotype XX and Xx compared to patients with genotype xx . A higher level of risk for operative treatment was observed among patients with genotype XX and Xx, compared to patients with genotype xx.

Polymorphism gene in adolescent idiopathic scoliosis

Ocaka *et al.* (2008) conducted a study aimed at relating angiotensin converting enzyme (ACE), and Alpha-actinin-3 (ACTN3) polymorphisms to AIS. This show that the insert (I)allele is more frequent in endurance athletes, while the delete (D)allele appears more often in strength and muscular explosion athletes. The variability of this polymorphism can affect the performance of certain muscle groups that act as a means of support for the spinal column. The paraspinal musculature plays a trunk support and movement role, and any significant changes affect patients with AIS, who have trunk deformity in the three planes and significant rotation. **Wajchenberg *et al.* (2013)** reported on genetic polymorphisms studies carried out on patients with AIS in an attempt to correlate alterations in certain proteins that might be related to the disease. The polymorphisms were related to the genes MATN1 in region 1p35 and CHD7 in region 8q12.1. The human genetic map contains at least 170 variant sequences of genes, which are related to the phenotypes of physical performance and of fitness related to health. These genes include the angiotensin-converting enzyme (ACE) gene, which is located on chromosome 17q23, composed of 26 exons and 25 introns. A common genetic variant in the ACE gene was described as absence or deletion (D allele) and presence or insertion (I allele) of 287 base pairs in intron 16. The genetic studies associated this polymorphism with health, sports, and also the genesis and maintenance of various diseases.The genotyping of the I/D polymorphism of the ACE gene was conducted using two specific primers (Primer,ACES 5'CTGGAGACCACTCCCATCCTTTCT3') (Primer,ACEAS5'GATGTGGCCATCACATTCGTCAGAT-3') this shows the sequence where polymorphism occurs in the gene. **Wise *et al.* (2000)** using a genome-wide association study (GWAS), successfully correlated the chromosome region 10q24.31 with the disease by locating the single nucleotide polymorphism (SNP). This region is within the region 10q, and contains the Drosophila lady bird genes (LBX1) gene. This gene was expressed in the dorsal region of the spinal cord and skeletal muscle, and also operates in somatosensory neurons. LBX1 was related to the etiology of the disease due to somatosensitive dysfunction. The DNA region also contains regulators of gene expression, which could influence the

manifestation of the disease depending on the polymorphism (TT, TC and CC) that is present. LBX1, and detected high levels of expression in the skeletal muscle, and spinal cords of adult, and fetal humans. **(Wajchenberg *et al.*, 2015) Ward *et al*, (2010)** reported that 53 SNPs were closely associated with AIS severity. The markers used for these SNPs are rs2449539, rs1437480, rs448013, rs10493083, rs16945692. Based on this study, a diagnostic kit was developed that predict the progression of Cobb's angle and was sold commercially. **Sharma *et al*, (2011)** genotyped the SNPs chromosome, 3p26.3, and. discovered other significant associations in their genome-wide association study (GWAS) for SNPs (rs2222973) in the Down syndrome cell adhesion molecule (DSCAM) gene. Common SNPs in the genes of matrilin 1 (MATN1) and insulin-like growth factor 1 (IGF1) are said to be associated with AIS in Chinese **(Moon *et al., 2013*).**

METHOD

This research work seek to gather all the genetic data on spinal cord disorders, then a comparative analysis was performed on the various types of genes and their biological factors which are the likely to cause scoliosis in either mutant or deficiency forms. Comparative analysis was done on the various genes and the biological factors that are susceptible to the causes of scoliosis.

Table 1 Showing Chromosomal Regional locations and their Gene types for Adolescent Idiopathic scoliosis disorders.

Chromosome Regional Locations for adolescent idiopathic scoliosis (AIS &IS)	Gene Type	Reference
$1p^{3.5}$	MATN1	Montanaro et al, 2006
$8q^{12.1}$-$q^{12.2}$	CHD_7	Arbanas. C., 2007; Zentner et al, 2010; Swarkar et at, 2010.
Xq	GATA	Carol et al, 2008,
6p,6q,8q,9q,10q,16q,17p,18q,19p	SNTG1	Carol et al, 2008,
$18q^{12.1\text{-}12.2}$	DTNA,	Christiana et al, 2009.
$3p^{26.3}$	B4GALT6,GALNT1, CHL1, ROBO3	Swarkar et al, 2010
10q24-31	LBX1	Tkahashi et al,2011
6p, 10q, 18q, 19p13.3, 17p11, $19p^{13}$, $8q^{12}$, $9q^{31.2}$, $q^{34.2}$, $17q^{25.3}$, 12p.	ESR1, ESR2, MATN1, MATNR1B	Gao et al, 2013
X_q	MANT1	Gao et al, 2013
$12p,17q^{25.3},18q^{12.1\text{-}12.2}$		Wajchenberg et al,2015

Table 2 shows the Full names of the various types genes associated with Adolescent Idiopathic scoliosis disorders.

Genes Type	Full name
MANT1	Matrilin 1, cartilage matrix protein
CHD_7	chromodomain helicase DNA binding protein 7
GATA	globin transcription factor
SNTG1	Gamma-1-syntrophin
DTNA	Dystrobrevin alpha
B4GALT6	Beta-1, 4-galactosyltransferase 6.
GALNT1	Polypeptide N-acetylgalactosaminyl transferase 1
CHL1	cell adhesion molecule L1
ROBO3	roundabout, axon guidance receptor, homolog 3 (Drosophila)
LBX1	Ladybird Estrogen Receptor 1Homeobox 1
ESR1	EStrogen Receptor 1
ESR2	EStrogen Receptor 2
MATNR1B	melatonin receptor 1B

Table 3 showing the number of occurrences of Chromosome types in the scoliosis disorder considering table 4.1above.

Chromosome number	Number of Occurrences
1	1
3	1
6	2
8	3
9	2
10	3
12	2
16	1
17	3
18	4
19	3
X	2

Table 4 comparing the p-arm (short) and the q-arm (long) of the chromosomes to determine which arm is more susceptible to scoliosis disorders. Considering the date from table 1

Chromosome number	p-arm number of occurrence	q-arm number of occurrence
1	1	-
3	1	-
6	2	1
8	-	3
9	-	2
10	-	3
12	2	-
16	-	1
17	2	2
18	-	4
19	3	-
X	-	2
Total	11	18

RESULTS

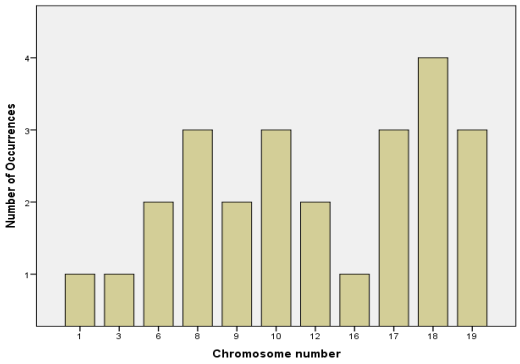


Figure 1 showing the number of occurrence of chromosome number

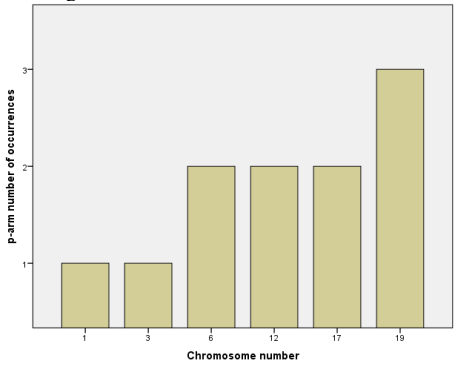


Figure 2 showing the number of occurrence of the p-arm in the scoliosis disorder chromosomes.

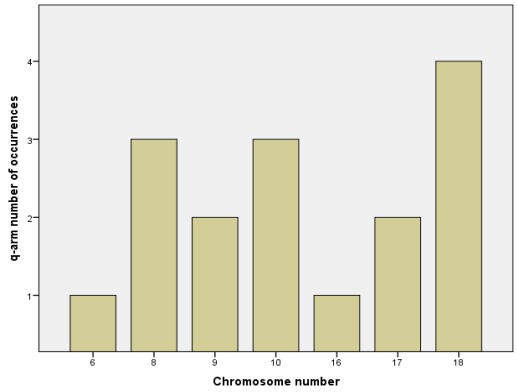
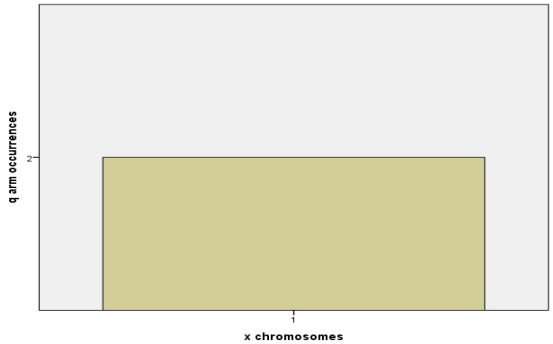


Figure 3 showing the number of occurrence of the q-arm in the scoliosis disorder chromosomes.

Figure 4 showing the number of occurrence of X-chromosomes number 1 represents X chromosome on the x axis

Figure 5 showing the number of occurrence of the p-arm in the scoliosis disorder of the X-chromosomes.



1 represent X chromosome x axis

Figure 6 showing the number of occurrence of the q-arm in the scoliosis disorder of the X-chromosomes

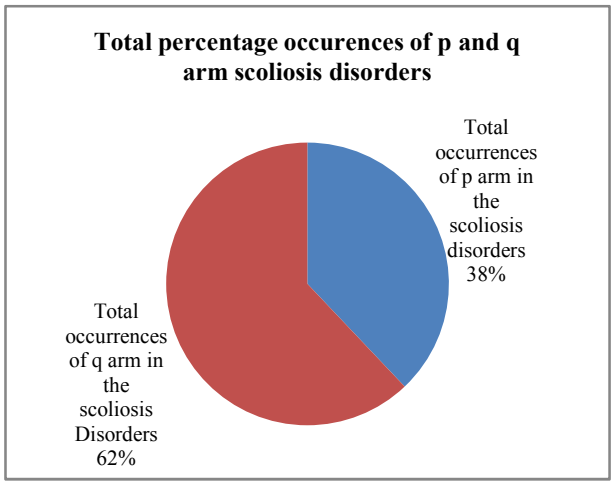


Figure 7 Pie Chart showing the total percentage occurrences of p and q arms of the chromosomes of the scoliosis disorders.

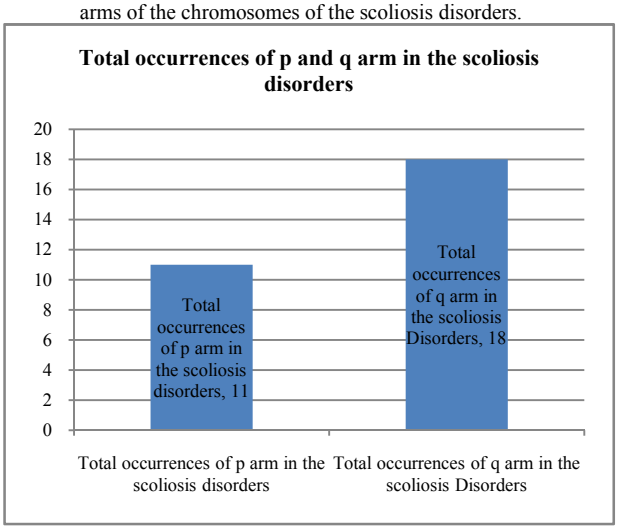


Figure 8 Total occurrences of p and q arms chromosomes it the causes of scoliosis disorders.

DISCUSSION

A scoliosis disorder occurs due to several factors and mostly it is by a Gene Abnormalities. Such abnormalities arises because of changes in the molecular biological systems of humans, These causes the degree of changes in the various internal structure components such as melatonin, calmodulin, and growth hormones levels to change. Table 2 shows the various abnormal genes that contribute to the Adolescent Idiopathic scoliosis disorders. Table 1 shows the sample data of the various research conducted by various researchers to determine which types of chromosomes in the human is susceptible to adolescent idiopathic scoliosis disorders. **Montanaro *et al*, (2006)** detected $1p^{3.5}$ chromosomes to be the chromosomal region for the occurrence of Adolescent Idiopathic scoliosis disorders. $8q^{12.1}$-$q^{12.2}$ chromosomal regions was identified by **(Arbanas. C., 2007; Zentner *et al*, 2010; Swarkar *et at*, 2010).**Regions on chromosomes 6, 9, 16, and 17 were considered to have the strongest evidence for linkage a cross all subsets of scoliosis-families studied **(Romaine *et al.*, 2013). Salehi *et al.* (2002)** found regions linking adolescent idiopathic scoliosis to chromosome17. **Carol *et al*, (2008)** also discovered chromosomal region 6p, 6q, 8q, 9q, 10q, 16q, 17p, 18q, 19p to

be susceptible to Adolescent Idiopathic scoliosis disorders. **Christiana *et al*, (2009),** fine out that chromosomal region number $18q^{12.1-12.2}$ is also a region for susceptible to adolescent idiopathic scoliosis disorders .Furthermore **Swarkar *et al*, (2010)** identified that chromosomal region $3p^{26.3}$ to be susceptible. 10q24-31 chromosomal location was discovered by **Tkahashi *et al*, (2011). Gao *et al*, (2013**), discovered a large number of chromosomal regional locations 6p, 10q, 18q, 19p13.3, 17p11, $19p^{13}$, $8q^{12}$, $9q^{31.2}$, $q^{34.2}$, $17q^{25.3}$, 12p. which are very much susceptible to susceptible to adolescent idiopathic scoliosis disorders (AIS).12p, 17q25.3, and $18q12.1^{-12.2}$ chromosomal region location was identified by **Wajchenberg *et al*, (2015).**

Heritable genes and genetic factors have been found to play a vital role in the occurrence and development of AIS which have been identified in genome-wide linkage studies conducted by **(Wenjie, 2013).** A genome-wide association study (GWAS) was performed in a Japanese population, and three SNPs (rs11190870, rs625039 and rs11598564), all of which were located near the gene LBX1 on chromosome 10q24.31 **(Wenjie *et.al*, 2013).** Male-to-male transmission is apparently rare and was specifically absent in 17 families studied by **Cowell *et al.* (1972**), who suggested X-linked dominant inheritance as it shown in the table 4.1above **Carol *et al*,(2008)** also identified Xq to be a heritable adolescent idiopathic scoliosis disorders. X_q was also discovered by **Gao *et al*, (2013)** as a heritable disorders from X-chromosomes.

Table 3 showing number of occurrences of a Chromosome types in the scoliosis disorder considering table 4.1above.It can be identified that chromosome number 18 was reported by four times by different researchers to be associated with susceptible to adolescent idiopathic scoliosis disorders. Chromosome numbers 19, 17, 10, 8 was reported to occur three times each in the table 1 chromosome numbers 12, 9, 6, and X occurred two times each from the data collected by researchers. Chromosomes numbers 16, 3, and 1 appeared one time each in their susceptibility to adolescent idiopathic scoliosis disorders. This shows that chromosome number 18 is more susceptible to adolescent idiopathic scoliosis disorders as reported by **(Carol *et al*, 2008; Christiana *et al*, 2009; Gao *et al*, 2013, and Wajchenberg *et al*, 2015**). This Followed by Chromosome numbers 19, 17, 10, and 8, then chromosome numbers 12, 9, 6, and X. The least susceptible Chromosomes numbers are 16, 3, and 1 which occurred once as reported by **(Montanaro *et al*, 2006; Carol *et al*, 2008; Swarkar *et al*, 2010).**

Comparing the p-arm (short) and the q-arm (long) of the chromosomes to determine which arm is more susceptible to scoliosis disorders from table 4 shows that the p-arm of the chromosome number 19 has the highest occurrence of three (3).This is also shown by the figure 2 and collaborated by the figure 3 showing p-arm to be three. The chromosomes number 18 shows that it has highest occurrences in its q-arm than the p-arm .Its q-arm occurred four (4) times and no occurrences appeared at its p –arms. Chromosomes number 8 and 10 has their q arms occurring three times with their p-arms occurring not appearing to contribute to the disorder. The total number of p-arm contributing to the scoliosis disorder by the chromosome numbers 1,3,6,8,9,10,12,16,17,18,19,and X is 11 whiles the total contribution of the q-arm by chromosome numbers 1,3,6,8,9,10,12,16,17,18,19,and X is 18 as it is represented in figure 7 and figure 8 respectively. From this analysis it shows clear that q –arms of the chromosomes in the humans are more susceptible to adolescent idiopathic scoliosis disorders than p-arms of the chromosomes. This is also can be confirmed from table 1 which shows that chromosome number 18 which has the highest occurrences of four (4) from the data collected to show the scoliosis disorders among the other chromosomes occurred at the q-arm as shown in figure 2 and 3, and nothing occurred at the p-arm. The least chromosomes number occurrence from table .1 are chromosomes 1, 3, and 16.Chromosomes number 1 and 3 occurred one time and it appear on p-arm whiles chromosome number 16 which occurred one time appeared on q-arm. This confirmed that p-arm is least susceptible to adolescent idiopathic scoliosis disorders in humans.

X-chromosomes inheritance is also determinate factor of scoliosis from parents to children as show in the table 4.1 of the collected data above .The number of X-chromosomes occurrence is two (2).This occurred on the q arm as shown in figure 6.The p arm chromosomes of x did not show any occurrences of scoliosis disorder as described in figure 4.9..This further confirms p arms are susceptible to scoliosis than p arm. If the scoliosis genes are located on the X chromosome this means that it will give rise to various disorders. Scoliosis is more common in females than males, at a ratio of 4:1.Males only has one X chromosome, whereas females have two (Justice *et al*., 2003). Polymorphisms which was related to the genes MATN1 in region 1p35 and CHD7 in region 8q12 also contributed to the scoliosis disorders in humans. This was confirmed by **Wise *et al*. (2000)** using a genome-wide association study (GWAS).

CONCLUSION

Though scoliosis can be term genetic disorder it is mostly acquired through various activities by the human subjects. The chromosomes number 18 shows that it has highest occurrences than others chromosomes in the human subject's .The q-arm contribute to scoliosis disorder than the p-arm. Scoliosis is prevalence among most active group between 18-70 years. Specially athletes, motor bike riders and office workers who sit down lots. Using very lighter, simple designed and fabricated buzzer device scoliosis can be detected earlier (mild and moderate levels) and controlled to prevent severe form of scoliosis which will lead to surgery.

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