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AN ASSESSMENT OF DEVELOPMENTAL ANOMALIES IN THE THORACO-LUMBO-SACRAL REGION OF SOUTH AFRICANS

By

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A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand,

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in fulfillment of the requirements for the degree of Master of Medicine



UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

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Abstract

Developmental anomalies, typically caused by epigenetic interactions, are very common in the human vertebral column. Many studies have been conducted to assess their prevalence in different populations. Several studies have shown differences in the prevalence and expression of vertebral anomalies among populations and between the sexes. These differences may be related to different geographical areas and the environmental conditions posed by these, socio-economic status, diets, lifestyles and/or gender roles, to name a few. Therefore, this study aimed at assessing the prevalence and pattern of six developmental anomalies in the thoraco-lumbosacral regions and their possible associations with vertebral pathologies in South Africans.

The study comprised skeletal remains of 902 individuals. The remains were procured from the Raymond A. Dart Collection of Modern Human Skeletons, the Pretoria Bone Collection and the Kirsten Bone Collection. The sample included South African Blacks (SAB) (*n*=325), South African Coloureds (SAC) (*n*=286) and South African Whites (SAW) (*n*=291). The most common vertebral developmental anomaly observed in this study was sacralisation (5.7%), followed by spina bifida occulta (4.5%), spondylolysis (4.5%), L6 (3.1%), and T13 (2.2%). The lowest prevalence was seen for lumbarisation at 1.9%. Overall, developmental anomalies were most prevalent in the SAB sample compared to the SAC or SAW. These anomalies were generally more prevalent in males of the total sample and within the three populations groups of the study. The high prevalence of most developmental anomalies in the SAB sample may be mostly related to the low socio-economic status associated with Black South Africans under the apartheid era.

The presence of multiple anomalies was more prevalent in Blacks (44.4%). Blacks also had a higher prevalence for multiple anomalies accompanied by some form of spinal pathology (50%). Whites, on the other hand, had a higher prevalence of a single developmental anomaly accompanied by some form of spinal pathology (50%). In general, males were more prone to developing multiple anomalies accompanied by some form of spinal pathology.

There was substantial variation observed with regards to the presentation of the six developmental anomalies in and between the samples under study. Therefore, inter- and intrapopulation differences, as well as sex differences, should be considered when dealing with the above developmental anomalies in biological anthropological and clinical settings.

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List of abbreviations

- SA: South Africa/ South African
- Hox: Homeobox
- LSTV: Lumbo-Sacral-Transitional - Vertebra
- LBP: Lower back pain
- T1: First thoracic vertebra
- T13: Thirteenth thoracic vertebra
- L6: Sixth lumbar vertebra
- SBO: Spina bifida occulta
- L1: First lumbar vertebra
- L2: Second lumbar vertebra
- L3: Third lumbar vertebra
- L4: Fourth lumbar vertebra
- L5: Fifth lumbar vertebra
- SAB: South African Black
- SAC: South African Coloured
- SAW: South African White
- DISH: Diffuse idiopathic skeletal hyperostosis
- S1: First sacral segment
- S2: Second sacral segment
- S5: Fifth Sacral segment
- NTD: Neural tube defect
- T2: Second thoracic vertebra
- T3: Third thoracic vertebra
- T5: Fifth thoracic vertebra
- T11: Eleventh thoracic vertebra
- T12: Twelfth thoracic vertebra

- n: Number
- p-value: Probability value
- STA: Sacral table angle

Chapter 1
INTRODUCTION

Variation in human skeletal anatomy is common. Population-level variation in the expression of developmental anomalies occurs as a result of inherent genetic variability and exposure to different environmental conditions (Barnes, 2012a). For this reason, it has been suggested that some populations are more prone to specific congenital and developmental anomalies (Allbrook, 1955; Barnes, 1994; Roberts and Manchester, 2005).

Congenital anomalies can be defined as structural manifestations occurring before birth that do not conform to normal anatomy (Barnes, 2008, Sadler, 2010). The term congenital anomaly is, however, properly restricted to anomalies only present at birth and usually present with a high infant mortality rate (Barnes, 1994). Hence the more inclusive term 'developmental anomaly' will be used in this study to accommodate those anomalies that manifest after birth and whose expression may be exacerbated by growth and development, or in some cases by functional stress or even trauma (Barnes, 1994, 2012a; Marcsik *et al*., 2002).

Developmental anomalies may present due to complete developmental failure (aplasia), partial development (hypoplasia) or over-development (hyperplasia) (Roberts and Manchester, 2005). In addition, they can range from minor to severe defects. The severe defects usually result in early fatalities, which makes it very rare for them to be observed in adult individuals (Barnes, 2012a).

Factors affecting developmental anomalies can either be of an intrinsic or extrinsic nature (Roberts and Manchester, 2005; Barnes, 2008, 2012a). Intrinsic factors are those that are genetically driven and directly alter the development of the foetus (Roberts and Manchester, 2005; Jacobs *et al*., 2006; Barnes, 2012a). These account for the majority (90%) of developmental defects (Barnes, 1994). The occurrence of these genetic anomalies is mostly due to mutations that occur during the early stages of development. They can also result from the interaction of recessive or dominant genes (Roberts and Manchester, 2005; Barnes, 2012a). In fact, studies focussing on embryology indicate that most of these anomalies are genetic in origin (Turnpenny *et al*., 2007; Larsen, 2015).

Extrinsic factors are environmental stressors and include viral infections affecting the mother (e.g., rubella, measles, herpes simplex virus, syphilis), exposures to chemicals (e.g., drugs, alcohol, valproic acid, thalidomide, lead, trimethadione), lack of sufficient nutrients (e.g., folic acids, zinc, selenium), hormones (androgenic agents), in-vitro fertilisation and radiation (Barnes, 1994, 2012a; Brent, 2004; Roberts and Manchester, 2005; Sadler, 2010). Extrinsic agents can pass through the placenta and alter the developing foetus to cause abnormal morphology (Sadler, 2010).

The origin of developmental disorders can be categorised into three main groups based on the type of genetic change involved. These include single gene disorders responsible for approximately a third of developmental anomalies, chromosomal anomalies which are responsible for about one out of twelve disorders, and multifactorial anomalies which account for the remaining, and majority, of developmental anomalies (Barnes, 1994:10). Multifactorial anomalies occur as a result of disrupted genetic regulatory mechanisms and usually appear during childhood or later in adulthood when exacerbated by environmental stressors - resulting in an epigenetic interaction (Barnes, 2012a; Roberts and Manchester, 2005). A good example of this is spondylolysis, a condition unlike other anomalies that only manifests later in life when the pars interarticularis fractures under repetitive stress. The multifactorial nature of most anomalies, therefore, makes it very difficult to determine their aetiologies (Roberts and Manchester, 2005).

It is important to note that epigenetic-related anomalies only interfere with human development at specific phases of cellular development (Roberts and Manchester, 2005, Barnes, 2012b). These phases include proliferation, migration, differentiation and regression of the developing cells (Barnes, 1994). During these phases, cells are at their maximum potential for differentiating and are extremely sensitive to disturbances (Barnes, 1994). As a result, it is possible for an individual to display multiple unrelated developmental anomalies (Roberts and Manchester, 2005).

The most common region for the occurrence of skeletal developmental anomalies is the vertebral column (Masnicova and Benus, 2003; Barnes, 2012a). Segmental borders, which include the cervico-thoracic, thoraco-lumbar, lumbo-sacral and sacro-coccygeal transitions, are frequently affected (Shore, 1930; Barnes, 2008, 2012a). At these locations, developmental

variants manifest as additional segments or transitional vertebra with morphological characteristics of one type of vertebra superiorly and a different type inferiorly (termed‘border shifting’) (Barnes, 2008). The cervico-thoracic border has been found to be more stable than the other borders and is thus rarely affected by border shifting and numerical variations (Willis, 1923; Barnes, 1994; Moore *et al*., 2014). The lumbo-sacral border, in contrast, is more commonly affected by developmental anomalies and especially by border shifting (Shore, 1930; Barnes, 1994; Masnicova and Benus, 2003).

There is great variation in the frequency of developmental spinal anomalies among populations and between males and females within populations (Eubanks and Cheruvu, 2009; Walters, 2016; Garg, 2017; Parashuram *et al*., 2017; Groza *et al*., 2018; Kim *et al*., 2018; Patra *et al*., 2018). The effect of many anomalies on normal functioning is largely unknown. Some anomalies may be exacerbated by heavy loading on the spinal column, but others appear to be non-symptomatic and not identified until images are taken for diagnostic purposes relating to other vertebral conditions or chronic pain.

With regard to potential environmental stress factors and developmental anomalies, Hou *et al*., (2018) postulated that populations residing in high-altitude areas tend to present with more development anomalies as they are exposed to low oxygen levels (hypoxia) compared to those in low-altitude areas. Furthermore, populations in northern regions tend to present with more caudal shifting, as seen in individuals with 25 pre-sacral vertebrae (Merbs, 1974).

It is, therefore, important to investigate the frequencies of developmental anomalies within and between populations with distinctly different ancestries to begin to understand the patterns of developmental anomalies in modern humans. The ancestral diversity of the South African population provides a good opportunity to accomplish this. Additionally, it will be informative to investigate any associations of spinal developmental anomalies with other vertebral pathologies, such as Schmorl’s nodes, verbral body compression, kyphosis and scoliosis among others, to ascertain if the presence of pathology is increased in individuals with anomalies.

1.1 Aim and objectives

1.1.1 Aim

To investigate the prevalence and pattern of developmental anomalies in the thoraco-lumbosacral elements of South African skeletal samples.

1.1.2 Objectives

- To determine and compare the prevalence of the following developmental anomalies in a southern African sample: vertebral border shifting, numerical variations, spina bifida and spondylolysis in the thoraco-lumbo-sacral region.

- To describe and compare the variations of each developmental anomaly observed within the study sample, and between males and females and different population groups.

- To determine if any association exists between the presence of the developmental anomalies studied here and other spinal pathologies (including Schmorl's nodes, compression of vertebral bodies, and kyphosis).

1.2 Hypotheses

There are three major hypotheses to be evaluated in this research, based on current understanding of developmental anomalies of the thoracic, lumbar and sacral components of the vertebral column:

1. Variation in the expression of developmental anomalies is mainly due to genetic variation and environmental exposures. Therefore, it is expected that the prevalence of developmental anomalies should vary among South African (SA) populations as they have different genetic histories.

2. The severity of developmental anomalies have been documented to vary between different sexes and populations. It is hypothesised that the vertebral developmental expression/severity will differ between males and females and the different SA population samples.

3. It is hypothesised that individuals with developmental anomalies in the thoraco-lumbosacral region are more likely to develop vertebral pathologies due to compromised normal anatomy and biomechanical changes in the vertebral column.

Chapter 2
LITERATURE REVIEW

2.1 Vertebral development

Vertebral developmental anomalies occur during embryogenesis, specifically during somitogenesis (Cordes *et al*., 2004; Kusumi and Turnpenny, 2007). The vertebral column mainly originates from the paraxial mesoderm which gives rise to 44 pairs of somites (Barnes, 1994; Kaplan *et al*., 2005; Sadler, 2010; Parashuram *et al*., 2017). These somites differentiate into three components, namely the myotome, dermatome and sclerotome. The latter is the crucial component in vertebral column formation (Barnes, 1994; Kaplan *et al*., 2005).

Sclerotome segments surround the notochord through migration (Barnes, 1994; Kaplan *et al*., 2005; Garg, 2017; Parashuram *et al*., 2017). These cells are then separated and arranged into a highly dense cranial portion and a less dense caudal portion (Barnes, 1994; Kaplan *et al*., 2005; Larsen, 2015). The intervertebral discs develop in between formed segments by the third month of foetal development (Kaplan *et al*., 2005, Sadler, 2010; Larsen, 2015). The sclerotome subsequently goes through resegmentation when the cranial and caudal halves fuse to form the vertebral body (Barnes, 1994, 2008, 2012a; Kaplan *et al*., 2005; Sadler, 2010; Larsen, 2015; Williams and Russo, 2015; Garg, 2017; Parashuram *et al*., 2017). The vertebrae subsequently differentiate and acquire characteristics specific to their region within the vertebral column (Barnes, 1994).

The Notch and Wnt signalling pathways, along with genes such as the Hox and Paired box genes (Pax), are crucial in regulating the embryonic development of the vertebral column (Mallo *et al*., 2010; Moore *et al*., 2016). They are responsible for the different morphological characteristics specific to each region. Disturbances in the expression of these genes may cause abnormal development and, therefore, the anomalies under study here (Peters *et al*., 1999; Pourquie and Kusumi, 2001; Carapuço *et al*., 2005; Kusumi and Turnpenny, 2007; Mallo *et al*., 2010; Sadler, 2010; Scaal, 2016; Garg, 2017; Abutaher and Avinash, 2019).

2.2 Vertebral morphology

The human vertebral column (Fig 1.1) typically consists of 33 segments including seven cervical, twelve thoracic, five lumbar, five fused sacral elements and four to five coccygeal vertebrae (Merbs, 1974; Barnes, 1994; Haeusler *et al*., 2002; White and Folkens, 2005; Sadler, 2010; Marieb and Hoehn, 2013; Martini *et al*., 2015; Scaal, 2016). In addition, the adult vertebral column has four main curvatures including the thoracic and sacral curvatures, also known as the kyphoses as they are convex posteriorly (Martini *et al*., 2015). The cervical and lumbar curvatures (the lordoses) are concave posteriorly. The cervical lordosis is responsible for head balance and forward eye positioning during an upright stance. As most of the human body's weight is situated anteriorly in an upright position, the lower curvatures act to bring the weight in alignment with the body's central axis (Martini *et al*., 2015:252).

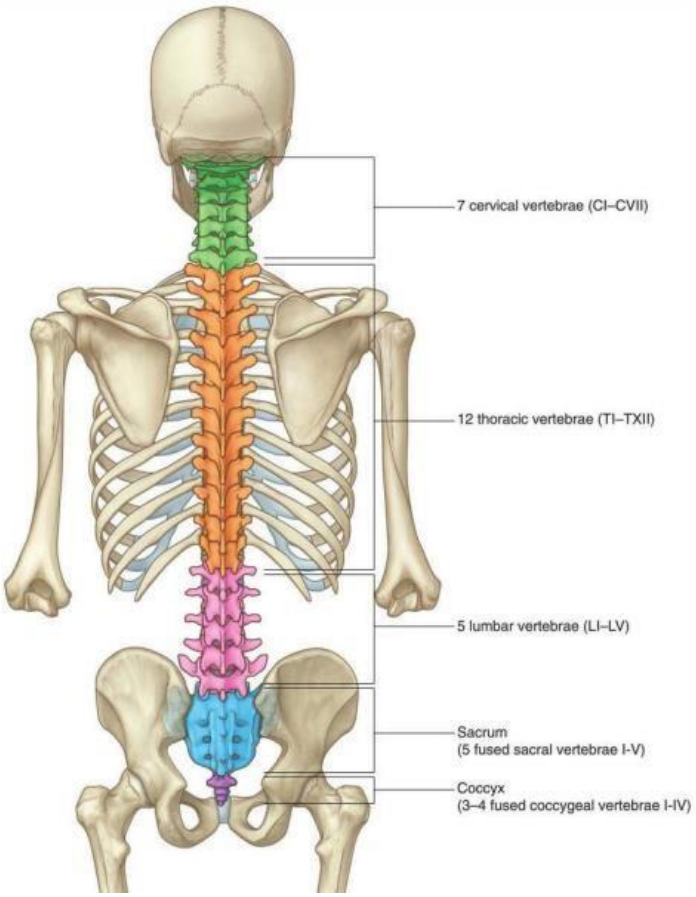


Figure 1.1: Different regions (coloured) of the vertebral column (Drake *et al*., 2015:56)

A standard (typical) vertebra is made up of a vertebral body and a vertebral arch (Drake *et al*., 2009, Martini *et al*., 2015). The common osteological features of a typical vertebra include the laminae that connect the vertebral arch to the vertebral body, pedicles that fuse to form the posteriorly placed spinous process, the postero-laterally placed transverse processes, the

superior and inferior articular processes with facets for articulation with adjacent vertebrae, and the vertebral foramen that houses the spinal cord (Fig 1.2) (White and Folkens, 2005; Drake *et al*., 2009; Martini *et al*., 2015).

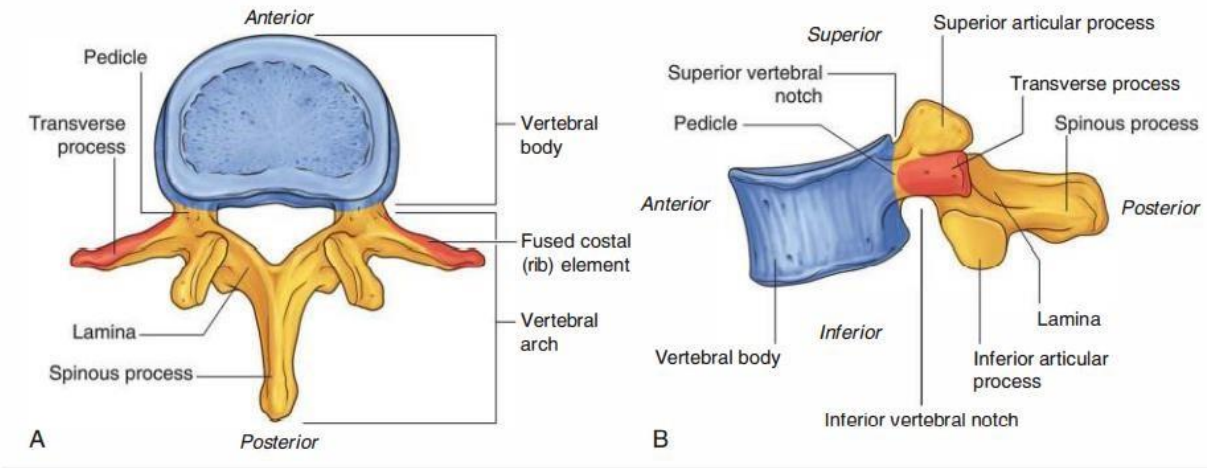


Figure 1.2: Typical (lumbar) vertebra (Drake *et al*., 2015:57).

Each of the segmental vertebrae (the cervical, thoracic, lumbar and sacral elements) has different morphological characteristics specific to their region and functions (Scaal, 2016). The morphology of the intervertebral articulations (the superior and inferior articular processes) and spinous processes vary by region, and this proves useful for identifying vertebral fragments. The cervicals are characterized by small bodies and bifid spinous processes (White and Folkens, 2005; Drake *et al*., 2015). They also have bilateral vertebral foramina that house the vertebral arteries that pass through to supply the brain (Drake *et al*., 2015). Costal facets are unique to the thoracic vertebra as they comprise the only region that articulates with the ribs (Drake *et al*., 2015). The lumbar vertebrae lack the costal facets and the vertebral foramina (White and Folkens, 2005; Drake *et al*., 2015). They have the largest vertebral bodies adapted for weight bearing (White and Folkens, 2005; Martini *et al*., 2015).

2.3 Vertebral developmental anomalies

Due to developmental disruptions, the number of regional vertebrae and the total number of vertebral segments may be reduced or increased (Nutter, 1913). The morphology of the vertebra may also be altered as a result of incomplete development (hypoplasia) or a complete lack of development of certain parts, termed aplasia (Roberts and Manchester, 2005).

2.3.1 Border shifting

Border shifting occurs in the spine as a result of upward or downward shifting of the segmental border (Barnes, 1994, 2008, 2012a, 2012b). This occurs when the sclerotomes separate into their respective caudal and cranial halves during embryonic development (Barnes, 2008; Dharati *et al*., 2012; Singh, 2014). As a result, the last or the first vertebral segment in the region assumes the morphological characteristics of the region above (cranial shift) or below (caudal shift) (Barnes, 1994, 2008, 2012a, 2012b). The vertebra affected by the cranial or caudal shift may undergo either a mild shift (when the vertebra is morphologically transitional between two regions) or a complete shift (where the anatomy is completely altered to the anatomical features of the vertebral region to which it has been incorporated).

2.3.1.1 Thoraco-lumbar border shifting

At the thoraco-lumbar border, cranial shifting results in the incorporation of the 12th thoracic vertebra into the lumbar region. The rib facets on the 12th vertebra disappear or appear small and indicate the absence of rib articulation (Barnes, 2012b). In case of a mild shift, the transitional inferior articular facet of the 12th thoracic vertebra will then occur on the 11th thoracic vertebra, but no other morphological changes are seen (Barnes, 2012b).

Caudal shifting results in the incorporation of the first lumbar vertebra into the thoracic region (Barnes, 2012b). The transverse processes of the lumbar vertebra may be altered to form articulating ribs, known as lumbar ribs (Masnicova and Benus, 2003; Barnes, 2012a, 2012b). These lumbar ribs do not usually produce clinical symptoms (Aly *et al*., 2016; Chengetanai *et al*., 2017), but if they are very large, they may cause lower back pain (Barnes, 2012a). Lumbar ribs have been previously confused with osteophytes and even fractured transverse processes when viewed radiologically (Mahajan *et al*., 2013). Furthermore, the presence of a lumbar rib may cause confusion when locating the kidneys to perform renal biopsy and nephrectomy as these procedures use the angle between the 12th thoracic vertebra and the first lumbar vertebra (Sujatha and Dhamodaran, 2016). Lumbar ribs have also been associated with caudal shifting (lumbarisation) at the lumbo-sacral border (Nakajima *et al*., 2013).

Cranial shifting in the thoraco-lumbar border has been reported for various modern and historical populations. In Merbs' (1974) study, the Eskimo sample presented with a 2.8% prevalence, whereas the Northern American Indians had a 7.1% prevalence (Merbs, 1974).

Conversely, caudal shifting is more variable in its expression with recorded ranges of 3% in an 11^{th}-12^{th} century Slovakian population (Masnicova and Benus, 2003) to a 40% prevalence in an Eskimo sample (Merbs, 1974).

2.3.1.2 Lumbo-sacral border shifting

The most common anomaly of the lumbo-sacral border is referred to as a Lumbo-Sacral Transitional Vertebra (LSTV) in the clinical literature (Dzupa *et al.*, 2014). The vertebral border can either move cranially or caudally affecting the morphology of the L5 or S1 vertebral segments (Roberts and Manchester, 2005; Barnes, 2012b).

A cranial shift at the lumbo-sacral border is termed sacralisation (Masnicova and Benus, 2003; Roberts and Manchester, 2005; Williams and Russo, 2015). With sacralisation, the fifth lumbar vertebra may become incorporated into the sacrum, resulting in a six-segmented sacrum (Merbs, 1974; Barnes, 1994, 2012b; Mahato, 2010; Moore *et al*., 2014; Williams and Russo, 2015; Groza *et al*., 2018). In some cases, only the transverse processes of the lumbar vertebra are sacralised, and they acquire the expanded morphology of the sacral alae (Merbs, 1974; Barnes, 1994, 2012b; Khairnar and Rajale, 2013; Bron *et al*., 2007; Dharati *et al*., 2012). The morphology of the transverse processes of the last lumbar vertebra may be affected on one side (unilateral) or both sides (bilateral) (Barnes, 2012a, 2012b; Dharati *et al*., 2012). These changes more often occur unilaterally, specifically on the right side (Barnes, 1994, 2012b).

When there is caudal shifting at the lumbo-sacral border, the first sacral segment may be separated from the sacral body. The result is known as lumbarisation (Barnes, 1994; 2012b; Bron *et al*., 2007; Mahato, 2010; Moore *et at*., 2014; Groza *et al*., 2018) where th first sacral segment will take on the appearance of the last lumbar vertebra (Merbs, 1974; Roberts and Manchester, 2005; Khairnar and Rajale, 2013). In general, cranial shifting or sacralisation occurs more frequently than caudal shifting or lumbarisation (Barnes, 1994; Mahato, 2010; Dharati *et al*., 2012). However, when lumbarisation occurs, it is generally more frequent in females than in males (Barnes, 1994).

The paralogous *Hox 10* and *11* genes are responsible for the formation of the lumbar and sacral vertebral segments, respectively. *Hox 11* is specifically a crucial component in the formation of the sacral vertebra. A study on transgenic mice documented that sacralisation occurs due to the overexpression of *Hox 11* in the paraxial mesoderm during development (Carapuco *et al*., 2005). This overexpression causes the 5th lumbar vertebra to fuse and acquire sacral morphological characteristics (Carapuco *et al*., 2005; Singh, 2012; Garg, 2017). The expression of the *Hox 11* gene group in the paraxial mesoderm is crucial to the formation of the sacrum as its absence results in the S1 acquiring lumbar morphological characteristics (lumbarisation) (Wellik and Capecchi, 2003). Furthermore, should the *Hox 10* gene be absent or inactive, and the lumbar vertebrae acquire thoracic characteristics (Wellik and Capecchi, 2003).

Lower back pain (LBP), first described as Bertolotti's syndrome in 1917, has been associated with sacralisation in some clinical literature (Olofin *et al*., 2001; Delport *et al*., 2006; Quinlan *et al*., 2006; Nardo *et al*., 2012; Tang *et al*., 2014); other studies have reported contradictory results suggesting no association between sacralisation and LBP (Van Tulder *et al*., 1997; Luoma *et al*., 2004; Bulut *et al*., 2013; Akinyi, 2018). Additional possible clinical complications of sacralisation and lumbarisation include sciatica (compression of the sciatic nerve), disc herniation and early degeneration of the vertebra above the sacralised/lumbarised vertebra. All of these may cause lower back pain (Elster, 1989; Barnes, 1994; Vergauwen *et al*., 1997; Luoma *et al*., 2004; Bron *et al*., 2007; Ravikumar *et al*., 2013; Sekharappa *et al*., 2014; Singh, 2014; Nayak, 2016). Furthermore, when the fifth lumbar vertebra is fused to the sacrum in sacralisation, it may result in a less mobile pelvis causing difficulties with partiuition (Dharati *et al*., 2012; Garg, 2017; Parashuram *et al*., 2017).

The early degeneration of the intervertebral disc with sacralisation can be detected in young individuals. In older individuals, however, it is difficult to determine if the disc degeneration is due to sacralisation or normal age-related degenerative changes (Patra *et al*., 2018). The early onset of intervertebral disc degeneration of lumbar vertebrae above the sacralised vertebra may subsequently cause nerve root compression, which may in turn cause pain in the lumbo-sacral region (Nayak, 2016).

There are only two types of sacralisation, as defined by Castellvi *et al*. (1974) that produce clinical symptoms. These are Type II and Type IV. Type II is associated with enlarged L5 transverse processes with unilateral or bilateral pseudoarthrosis with the sacral ala. Type IV characterises cases with the complete union of the last lumbar vertebra and the sacrum on one side, and incomplete union on the other side (Castellvi *et al*., 1974; Nardo *et al*., 2012; Tang *et al*., 2014). Therefore, if there is no pseudo-arthrosis between the sacralised vertebra and the alae of the sacrum, it is unlikely there will be clinical presentation of LBP and/or nerve impingement causing sciatica (Nardo *et al*., 2012).

The known prevalences of sacralisation range from 1.48% in ancient Egyptians (Sarry El-Din and El Banna, 2006) to 19% in ancient Pompeiians (Henneberg and Henneberg, 1999) in dry bone studies. In radiological studies of modern populations, the prevalence ranges from 4.1% (Australians) (French *et al*., 2014) to 82% (Ugandan) (Akinyi, 2018) (Appendix 1, Table A1).

Sacralisation has been most comprehensively studied among Indian populations and the majority of these studies indicate a higher prevalence in males (Sharma *et al*., 2011; Dharati *et al*., 2012; Deepa and Martin, 2013; Garg, 2017; Patra *et al*., 2018). African-based studies have also reported a higher prevalence in males (Olofin *et al*., 2001; Walters, 2016). There are only a few studies that have reported a higher prevalence of sacralisation in females for both dry bone (Sarry El-Din and El Banna, 2006) and MRI scans (Tins and Balain, 2016), suggesting a comparative rarity of this anomaly in females.

The prevalence of lumbarisation ranges from 0% in the Devı ´n-Za kostolom sample from Slovakia (Masnicova and Benus, 2003) to 36% in Lagos, Nigeria (Olofin *et al*., 2001) (Table A2). In contrast to the pattern in sacralisation, females tend to present with a higher prevalence of lumbarisation than males (Olofin *et al*., 2001; Dharati *et al*., 2012; Ucar *et al*., 2013; Patra *et al*., 2018). However, some studies reported a higher prevalence in males (Sharma *et al*., 2011; Tins and Balain, 2016; Groza *et al*., 2018), whereas another reported equally low prevalences in males and females of the ancient Egyptians (Sarry El-Din and El Banna, 2006).

Most studies report higher prevalences for sacralisation than lumbarisation in populations (Olofin *et al*., 2001; Masnicova and Benus, 2003; Sharma *et al*., 2011; Dharati *et al*., 2012; Deepa and Martin, 2013; Ucar *et al*., 2013; Tins and Balain, 2016; Groza *et al*., 2018). However, some variability exists as the Eskimo and Australian populations have lower sacralisation prevalences (Merbs, 1974; French *et al*., 2014). Equal prevalences of sacralisation and lumbarisation were reported for the Imphal and Mumbai Indian samples (Singh and Singh, 2015; Abutaher and Avinash, 2019). In these studies, the sample sizes were rather small (Imphal *n*=30, Mumbai *n*=98).

2.3.2 Numerical variation

An extra vertebra (also termed a supernumerary or transitional vertebra) may be present at the vertebral borders. This affects not only the number of the regional vertebra but also the total number of vertebrae in the column (Barnes, 1994). Similar to what occurs in border shifting, the transitional vertebra can take on the characteristics of either the vertebra above or below the border or can present with features of both borders (Barnes, 2008, 2012b).

According to Tague (2018), the main cause of supernumerary vertebrae is somitogenesis and homeotic transformation. When the process of somitogenesis gets interrupted by teratogenic effects or the inactivation of certain genes, the result is a change in segmentation of the vertebrae that may result in a supernumerary vertebra (Tague, 2018). Homeotic transformation refers to the change in the positional identity of a vertebra, which affects the regional count, but not the total number of vertebrae (Tague, 2018). Maternal hyperthermia, the condition where infection response or extreme environmental conditions raise the mother's core temperature, has been suggested as a possible aetiology of homeotic transformation (Oostra *et al*., 2005).

Reduction of the normal number of 24 presacral vertebrae to 23 is rare. Prevalences ranging from 0% to 6.3% are reported, with the South African San population showing the lowest at 0% (De Beer Kaufman, 1974) and Black North Americans showing the highest prevalence (6.3%) (Bornstein and Peterson, 1966). Increase in the presacral vertebral number to 25 segments seems to be more common with prevalences ranging from 2.6% to 14.3% amongst different populations (Allbrook, 1955; Bornstein and Peterson, 1966; De Beer Kaufman, 1974,

Tague, 2018). The 25-segment vertebral column is more frequently seen in males, whereas females present more with a 23-segment vertebral column (Tague, 2018).

With regards to a supernumerary 13th thoracic vertebra, the prevalences are between 2.6% and 15.7% (Table A3), with South African Blacks showing the lowest prevalence (2.6%) (De Beer Kaufman, 1974) and Sadlermiut Eskimos showing the highest prevalence (15.7%) (Merbs, 1974). The supernumerary 13th thoracic vertebra is reported to be more prevalent in South African Black and San males compared to females (De Beer Kaufman, 1974), while the difference between males and females was not statistically significant for African Americans and European Americans (Tague, 2018).

The Sadlermiut Eskimo population presented with a low prevalence of supernumerary sixth lumbar vertebra of 4.3%, whereas the South African San population was determined to have a higher prevalence of 14.3% (Refer to Table A4 in the appendix). Males had a higher prevalence of both conditions in the South African Black (L6=10.5%; T13=3.6%) and San populations (L6=10.7%; T13=3.6%) (De Beer Kaufman, 1974). For South African Blacks, the prevalence of general numerical variation was previously found to be higher in males (Shore, 1930; De Beer Kaufman, 1974, 1977).

- **Spina bifida**

Spina bifida is a neural tube defect (NTD) that results in the incomplete development (hypoplasia) or absence (aplasia) of posterior neural arches and/or spinous processes (Shore, 1930; Barnes, 1994; Masnicova and Benus, 2003; Ortner, 2003, Roberts and Manchester, 2005). Two main types of spina bifida are recognized clinically: spina bifida systica and spina bifida occulta (SBO) (Roberts and Manchester, 2005). Spina bifida systica involves the protrusion of the spinal cord, nerve roots and meninges through the cleft arch, and the severest form is usually fatal (Ortner, 2003; Roberts and Manchester, 2005; Barnes, 2012a).

SBO is the milder form of spina bifida that does not involve protrusion of spinal tissues (Saluja, 1988; Kaplan *et al*., 2005; Roberts and Manchester, 2005; Josan *et al*., 2008; Barnes, 2012a). With SBO, the affected area is enclosed by skin and this does not usually cause life-threatening

clinical problems. Some individuals with SBO may experience motor function disorders, sphincter control problems, lowered perception of pain, lower back pain that is usually transferred to the lower limbs, and weakness in the lower limbs (Saluja, 1988; Barnes, 1994; Roberts and Manchester, 2005; Josan *et al*., 2008; Kumar and Tubbs, 2011; Simalcsik *et al*., 2011; Ali *et al*., 2014). Moreover, urologic symptoms such as recurring infection of the urinary tract and incontinence have been specifically associated with SBO in adults (Josan *et al*., 2008).

The aetiology of spina bifida has been linked to both genetic and environmental factors (Josan *et al*., 2008; Molto *et al*., 2019). Altintas *et al*. (2009) argued for a genetic basis. In their study, two siblings with spina bifida had a deletion of the same chromosome. Maternal folate deficiency is the most widely recognised risk factor among the non-genetic aetiologies (Josan *et al*., 2008, Biswal *et al*., 2018; Oumer *et al*., 2020; Kancherla *et al*., 2021). Other conditions such as maternal obesity, diabetes, and intake of anticonvulsants during pregnancy are associated with a higher risk of giving birth to a child with neural tube defects (Josan *et al*., 2008).

Spina bifida occulta prevalences range from 1.55% to 34.5% (Refer to Table A5 in the appendix). In North America, White individuals (14.2%) show a higher prevalence as opposed to Black individuals (9.8%) (Eubanks and Cheruvu, 2009). It has also been reported that males tend to be more affected by SBO than females (Fidas *et al*., 1989; Bradtmiller, 1974; Masnicova and Benus, 2003; Eubanks and Cheruvu, 2009; Groza *et al*., 2018; Kim *et al*., 2018; Molto *et al*., 2019). The spina bifida prevalences from different studies indicate that variation exists between and within populations (Molto *et al*., 2019).

Spondylolysis

Spondylolysis refers to the unilateral separation of the vertebral body from the arch at the pars interarticularis between the superior and inferior articulating facets (Lester and Shapiro, 1968; Bridges, 1989; Arriaza, 1997; Merbs, 2002; Mays, 2006; Syrmou *et al*., 2010; Leone *et al*., 2011; Pilloud and Canzonieri, 2014; Nakayama and Ehara, 2015; Gagnet *et al*. 2018). The condition commonly occurs on the lumbar vertebra, and 95% of cases involve L5 (Haukipuro, *et al*., 1978; Bridges, 1989; Merbs, 1989; Arriaza, 1997, 2002; Roberts and Manchester, 2005; Mays, 2006; Nakayama and Ehara, 2015).

Spondylolysis may sometimes progress into spondylolisthesis, a condition in which the pars interarticularis fractures bilaterally (Shore, 1930; Merbs, 1989, 2002; Arriaza, 1997; Ortner, 2003; Roberts and Manchester, 2005; Syrmou *et al*., 2010; Leone *et al*., 2011; Mora-de Sambricio and Garrido-Stratenwerth, 2014). In spondylolisthesis, there is anterior displacement of the vertebral column superior to the affected vertebral segment. This usually results in lower back pain (LBP) (Roberts and Manchester, 2005; Mays, 2006; Syrmou *et al*., 2010; Leone *et al*., 2011; Nakayama and Ehara, 2015; Gagnet *et al*., 2018).

The causative factors underlying spondylolysis are not fully understood. Unlike the anomalies discussed previously, spondylolysis only occurs after birth and is associated with upright posture (Roberts and Manchester, 2005; Mora-de Sambricio and Garrido-Stratenwerth, 2014; Plomp *et al*., 2020). Spondylolysis usually starts developing when a child begins walking (Roberts and Manchester, 2005). The role of bipedalism in spondylolysis is supported by Rosenberg *et al*. (1981), who found an absence of the condition in individuals who had never walked. In Frederickson *et al*.'s (1984) prospective study of Americans, the incidence of spondylolysis was 4.4% in 6-year-old children. At the age of 12 years there were eight additional individuals presenting with spondylolysis increasing the incidence to 5.4%. This incidence further increased to 6% in adults. In contrast, young Brazilians showed a high prevalence of 54.2% compared to the middle-aged (33.3%) and older adults (12.5%) (Lessa, 2011). These findings suggest that differences exist in the prevalence and patterning of spondylolysis and point to different triggering factors or possibly survivorship, but the onset in childhood is clear.

The prevalence of spondylolysis, and especially spondylolisthesis, is high in adolescents and young adults (Mays, 2006; Gagnet *et al*., 2018). This may be due to the reduced strength of the pars interarticularis in the lumbar region in the young (Gagnet *et al.* 2018). Another possible reason, stipulated by Mora-de Sambricio and Garrido-Stratenwerth (2014), may be that the posterior arch of the lumbar vertebrae is not yet fused, making it more prone to fractures and therefore spondylolysis. It has also been suggested that the growth plates of the lumbar vertebrae in adolescents and young adults are not completely ossified making those elements more vulnerable to slippage (anterior displacement) and subsequent spondylolisthesis (Gagnet *et al*., 2018).

According to Arriaza (1997), spondylolysis is brought about by the everyday life activities related to bipedalism and not necessarily bipedalism alone. A movement such as hyperextension of the spine, which increases lordosis of the lumbar vertebrae, is a feature unique to humans and may contribute to the development of spondylolysis (Arriaza, 1997; Ward and Latimer, 2005). Mays (2006), however, posits that spondylolysis could be a result of repetitive weight bearing on the lumbar vertebrae and may not be directly linked to any specific type of anatomical movement. Spondylolysis is reported to be high in athletes such as gymnasts, dancers, divers, wrestlers, rowers, throwers, boxers, swimmers, and golfers (Soler and Calderon, 2000; Syrmou *et al*., 2010). These athletic activities are associated with movements such as hyperextension and rotation of the spine (Nyska *et al*., 1999; Soler and Calderon, 2000). This research lends support to Arriaza and others who favour the movement hypothesis (Arriaza, 1997; Soler and Calderon, 2000; Ward and Latimer, 2005). The contradictory suggestions and findings of different authors indicate the complexity and the multifactorial nature of spondylolysis.

In addition, Arriaza (1997) hypothesized that it is possible that individuals with a greater lordotic curve could be more prone to spondylolysis. Lumbar lordosis and other pelvic parameters such as pelvic tilt and pelvic incidence are found to be statistically higher in individuals presenting with spondylolisthesis in radiological studies (Vialle *et al*., 2007; Oh *et al*., 2009; Chung *et al*., 2012). Variation in the progressive increase of the lumbar interfacet distance from L1 to L5 has been proposed to be another factor for developing spondylolysis and spondylolisthesis. Individuals with an increase in interfacet distance inferiorly (from L1S1) are less likely to develop spondylolysis making those who's lumbar interfacet distance does not increase inferiorly more prone to developing spondylolysis (Ward and Latimer, 2005; Ward *et al*., 2010; Chung *et al*., 2012).

In most cases, spondylolysis is asymptomatic and usually found by accident when patients are treated for other conditions (Roberts and Manchester, 2005; Syrmou *et al*., 2010; Mora-de Sambricio and Garrido-Stratenwerth, 2014; Nakayama and Ehara, 2015; Sakai *et al*., 2016; Gagnet *et al*., 2018). Spondylolysis cases are typically not identified, especially in the early stages (Weiss, 2009; Mora-de Sambricio and Garrido-Stratenwerth, 2014). This may be one

reason why most patients only realize they have the defect in the late stages when it has already progressed to spondylolisthesis.

Few individuals with spondylolysis complain of lower back pain (Eisenstein, 1978; Cheung *et al*., 2018), whereas individuals presenting with advanced spondylolisthesis may, in addition to LBP, present with spinal stenosis or pain radiating to the lower limbs due to the disturbances to the L5 nerve root (Eisenstein, 1978; Mora-de Sambricio and Garrido-Stratenwerth, 2014). Also, due to the anterior displacement of the L5 vertebra in spondylolisthesis, the size of the pelvic inlet decreases, which may result in difficulties during a natural birth (Nutter, 1913).

Individuals with spondylolysis who participate in sports, however, present with LBP (Soler and Calderon, 2000; Kulling *et al*., 2014; Zehnder *et al*., 2009; Sakai *et al.*, 2016). This shows that there are other factors, such as genetic predisposition and activity that contribute to the aetiology of spondylolysis and potential clinical manifestation or complications (Roberts and Manchester, 2005). To support this, the condition has been reported in familial studies (Haukipuro *et al*., 1978; Wynne-Davies and Scott, 1979; Young and Koning, 2003; Yamada *et al*., 2013).

The prevalence of spondylolysis, like other developmental anomalies, greatly varies among populations. Prevalences ranged from 0% in a modern Ohio population of non-ambulatory patients to 45% in the Alaskan Tigara population (Lester and Shapiro, 1968; Rosenberg *et al*., 1981) (Refer to Table A.6 in the Appendix). The highest prevalence has thus far been recorded among an Eskimo sample (45%) (Merbs, 1974). Most studies identified a higher prevalence in males (Gunness-Hey, 1981; Bradtmiller, 1974; Fibiger and Knüsel., 2005; Weiss, 2009; Pilloud and Canzonieri, 2014; Sakai *et al*., 2016; Kim *et al*., 2018), whereas some studies indicated the opposite (Bridges, 1989; Waldron, 1991). In the South African population, Eisenstein (1978) found a higher prevalence in males (3.5%) than females (2.6%) for a Black sample, and a higher prevalence in the White female sample (5.7%) compared to the White males (3.8%).

Unilateral spondylolysis has been described as one of the possible complications of spina bifida occulta in cases where there is pressure on the lumbar neural arch cleft (Barnes, 2012b).

The association between spondylolysis and spina bifida occulta has been described by several authors (Fredrickson *et al*., 1984; Oakley and Carty, 1984; Eisenstein, 1978; Waynnes-Davies and Scott, 1979; Mora-de Sambricio and Garrido-Stratenwerth, 2014). However, Mays (2006) did not find any association between the presence of spina bifida occulta and spondylolysis in a Medieval English sample.

Chapter 3
MATERIALS AND METHODS

3.1 Sample

The study sample consisted of the skeletal remains of 902 individuals representing various southern African populations. A sample size calculation for a quantitative cross-sectional study, based on a 95% confidence interval, was used to obtain the minimum sample size (Zar, 2010). In order to make this calculation, the prevalences of five different anomalies (sacralisation, lumbarisation, spina bifida occulta, spondylolysis and supernumerary vertebra) from an earlier pilot study on the same populations were evaluated. The highest prevalence of 22% sacralisation from the Black South African population, with the lowest corresponding 6% from the other populations, was used for the sample size calculation. The minimum total study sample required was calculated to be 750 individuals. This means that for each of the three South African ancestry groups a minimum of 250 individuals was required.

The study sample included individuals representative of southern African Black (SAB) (*n*=325), South African White (SAW) (*n*=291) and South African Coloured (SAC) (*n*=286). The age of the sample ranged from 13 to 89 years (Fig. 3.1). Both males and females were included and were distributed among the three population groups (Fig. 3.2). The sample was obtained from the following collections: the Raymond A. Dart Collection of Modern Human Skeletons housed in the School of Anatomical Sciences, Faculty of Health Sciences at the University of the Witwatersrand; the Pretoria Bone Collection in the Department of Anatomy, University of Pretoria and the Kirsten Collection, Division of Clinical Anatomy, University of Stellenbosch.

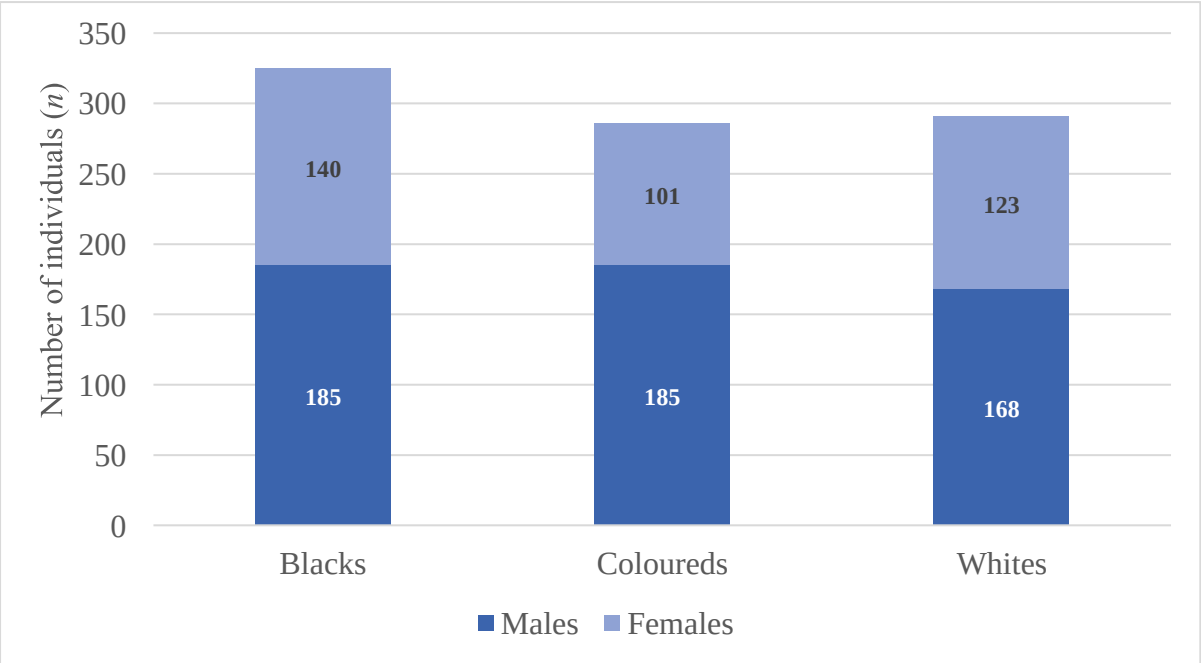


Figure 3.1: Distribution of the three subsamples

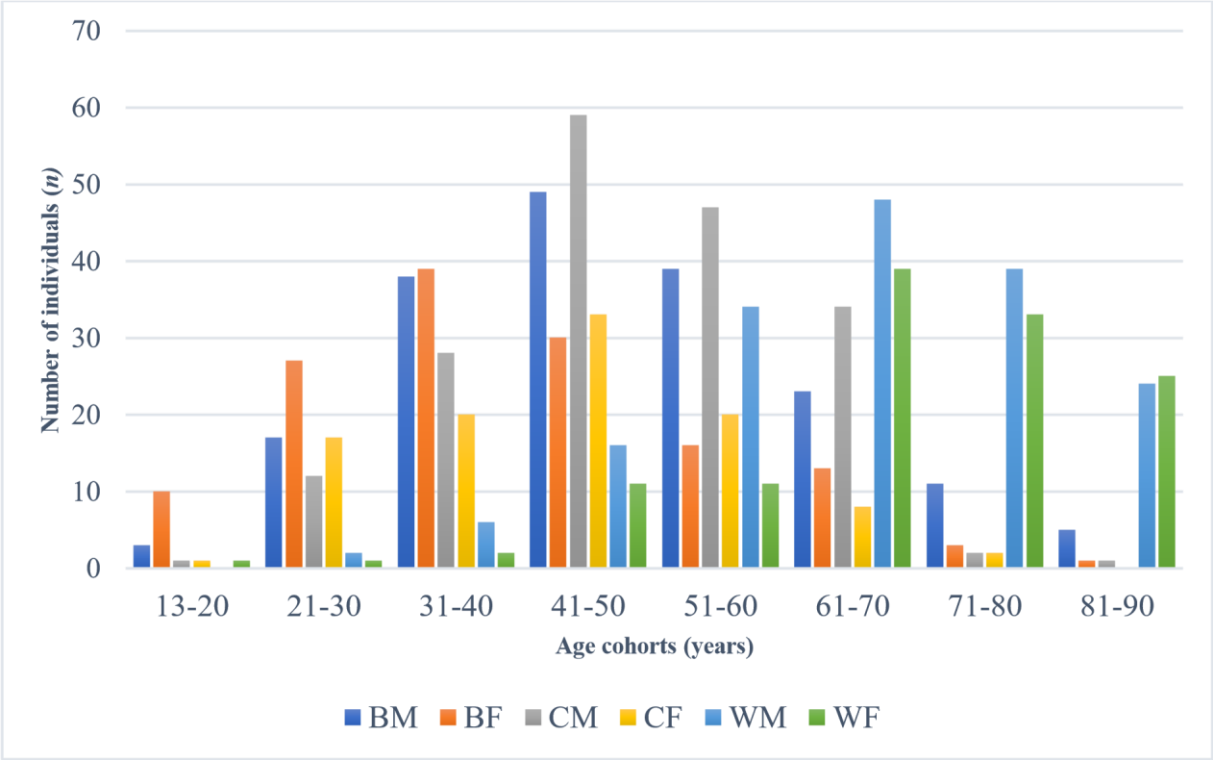


Figure 3.2: Age and sex distributions of the three subsamples

The Raymond A. Dart Collection of Human Skeletons is one of the largest cadaveric skeletal collections in the world (Dayal *et al*., 2009). The skeletons are mainly representative of individuals originating in South Africa (Dayal *et al.*, 2009). A large proportion of the collection is represented by southern African Black individuals, who were mostly unclaimed individuals from national hospitals (Dayal *et al*., 2009). These proportions have changed much since 2009 with almost all the newly accessioned individuals representing South African White individuals. The Pretoria Bone Collection is a rather small but growing skeletal collection with SAB and SAW individuals represented (L'Abbe *et al*., 2004). The Kirsten Collection houses the largest South African Coloured population sample in the world, and most of the skeletal materials were donated (Labuschagne and Mathey 2000; Alblas *et al*., 2018). The majority of skeletal remains in these collections are derived from cadaveric materials (Labuschagne and Mathey 2000; L'Abbe *et al*., 2004; Dayal *et al*., 2009; Alblas *et al*., 2018). The differing demographics of the subpopulations are evident in Figures 3.1 and 3.2, but every effort was made to sample comprehensively where possible.

3.1.2 Inclusion and exclusion criteria

Individuals with missing vertebrae or damage to the areas of interest in the thoraco-lumbosacral region were excluded from the study. Individuals with vertebrae affected by pathological lesions other than those considered in the study were also excluded (e.g., tuberculosis, multiple myeloma, DISH etc.).

3.2 Methods

The skeletal elements that were assessed included the thoracic, lumbar and sacral vertebrae. The vertebrae were carefully articulated to ensure the correct succession of the segments and to observe any associated pathology related to scoliosis and/or kyphosis. Correct articulation was identified when the inferior and superior articular facets presented with a tight fit. These elements were then visually examined to identify the developmental anomalies of border shifting, supernumerary vertebrae, spina bifida occulta and spondylolysis and the other non dev-elopmental spinal pathologies of interest (Schmorl's nodes, vertebral body compression, kyphosis and scoliosis). Photographs were taken using a Canon EOS 450D EFS 18-55 mm lens to illustrate observed developmental anomalies.

3.2.1 Sacralisation

Sacralisation was identified by the presence of six fused sacral segments, excluding any coccygeal segments that may be fused with the sacrum (Barnes, 2008). The condition was classified into three types using a modified version of Castellvi *et al*. (1984:493-494) (Table 3.1). A score of 1 indicated incomplete, unilateral sacralisation (Fig. 3.3), characterised by an enlarged transverse process without any bony union with the adjacent sacral ala. In cases of a bilateral occurrence, a score of 2 was given. Scores 1 and 2 were classified as Type I. Type II included scores 3 and 4, where score 3 represented complete unilateral sacralisation characterised by an enlarged transverse process, with bony union with the adjacent sacral alae. A score of 4 was given for a bilateral occurrence (Fig. 3.4A). Lastly, a score of 5 indicated a mixed feature, characterised by incomplete sacralisation on one side, and complete sacralisation on the other. This fell under Type III sacralisation. Additionally, it was noted whether fusion of sacral segments occurred on the left or right sides (Fig. 3.4B).



Figure 3.3 Incomplete, unilateral sacralisation. Arrow indicates an enlarged transverse process on the right. Anterior view. Type IA (AN398).

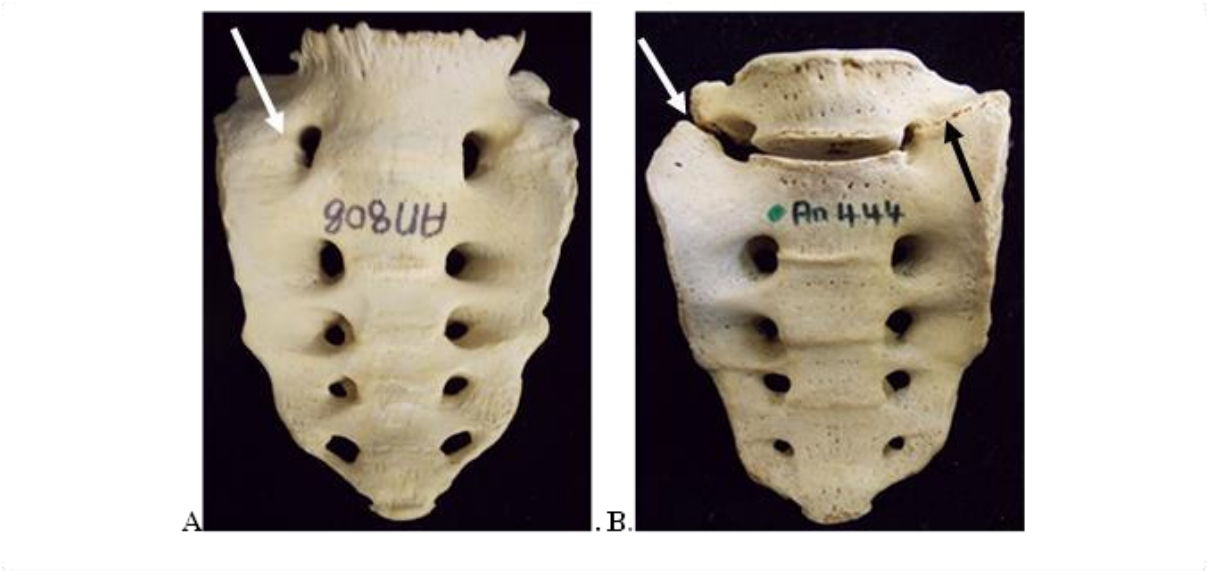


Figure 3.4: (A) Bilateral complete sacralisation Type IIB (complete fusion indicated by the two white arrows), (B) Mixed feature, Type III (The black arrow indicates partial fusion whereas the white arrow indicates no fusion). Anterior views.

Table 3.1: Sacralisation scoring criteria.

Type	**(Score)**	**Description**
Absent	0	No evidence of cranial shifting
Type I: A: Unilateral B: Bilateral	**Type IA** Unilateral- (1) **Type IB** Bilateral- (2)	Incomplete sacralisation is characterised by an enlarged transverse process without any bony union with the adjacent sacral ala
Type II: A: Unilateral B: Bilateral	**Type IIA** Unilateral- (3) **Type IIB** Bilateral- (4)	Complete sacralisation characterised by an enlarged transverse process with complete fusion with the adjacent sacral ala
Type III	(5)	Mixed feature with unilateral Type I on one side and unilateral Type II on the other

3.2.2 Lumbarisation

Lumbarisation is represented by the complete or incomplete separation of the first sacral segment (S1) from the sacral body. This coincides with an increase in the number of lumbar vertebrae to six, and the reduction of sacral body segments to four (Barnes, 2008). Moreover, the sacrum of a completely lumbarised vertebra appears shorter and wider with sacral alae that are higher than the promontory (Barnes, 2012b). The alae of the lumbarised S1 vertebra appear similar to the transverse processes of the lumbar vertebra in relation to shape and size, and in some cases, they may articulate with the alae of the sacrum (Barnes, 2012b). Lumbarisation is further classified into complete or incomplete separation of the first sacral body from the adjacent sacrum. A score of 1 was assigned in cases where lumbarisation was unilaterally incomplete (Fig. 3.4A). When it was incomplete bilaterally, a score of 2 was given. Therefore, both scores 1 and 2 were classified as Type I lumbarisation. A score of 3 was assigned in cases of complete lumbarisation, which is the complete separation of the first sacral segment from the adjacent sacrum (Fig. 3.5B). Score 3 was then classified as Type II lumbarisation. For a summary of descriptions associated with each of the lumbarisation types refer to Table 3.2.

Table 3.2 Lumbarisation scoring criteria.

TYPE	**Score**	**Description**
Absent	0	No evidence of caudal shifting
Type I . Unilateral . Bilateral	Type IA Unilateral- 1 Type IB Bilateral- 2	Incomplete lumbarisation, incomplete separation of the first sacral body from the adjacent sacrum, presented by an anterior cleft on the anterior aspect of the sacral body
Type II	3	Complete lumbarisation, complete separation of the first sacral segment from the adjacent sacrum, presented by the absence of a bony union

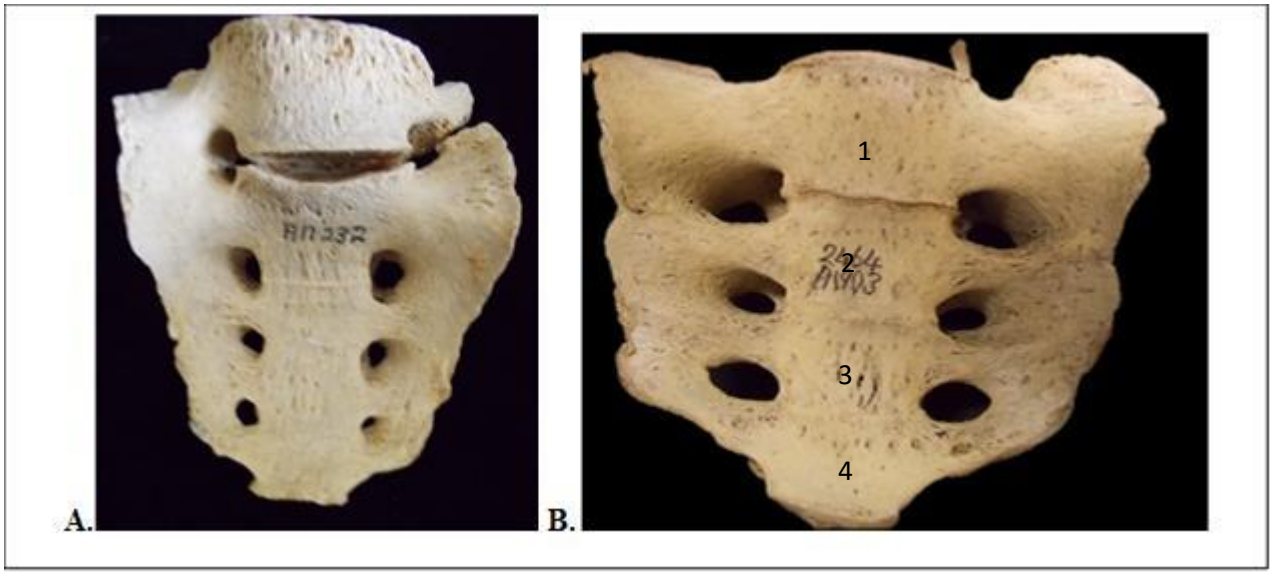


Figure 3.5: (A) Incomplete lumbarisation, Type IA. Arrow indicates the area of incomplete fusion (AN232). (B) Complete lumbarisation, Type II- the sacrum has four segments instead of five. Anterior views (A1903).

3.2.3 Supernumerary vertebra

Supernumerary vertebrae were identified from observation of the completely articulated column. The 13th thoracic and 6th lumbar vertebrae were identified by the presence of an extra vertebra at the thoraco-lumbar and lumbo-sacral borders, respectively (Barnes, 2012b). A score of 0 was allocated for the absence of an extra vertebral segment and a score of 1 was given where there was a 13th thoracic or sixth lumbar vertebra (See Tables A9 and A10 in Appendix 2, respectively). The extra vertebral segments may take on characteristics of both sides of the border or may only present with characteristics of the border above or the border below (Barnes, 2012a; 2012b).

3.2.4 Spina bifida occulta

Spina bifida occulta (SBO) presents as the absence of the posterior neural arches and/or spinous processes in the lumbo-sacral region (Roberts and Manchester, 2005). According to Barnes (1994), in palaeopathological studies SBO is often confused with cleft neural arches, a condition with a different aetiology. The confusion occurs because both SBO and cleft neural arches occur in the lumbosacral region. Barnes proposed that SBO with a neural tube defect (NTD) can be identified by the presence of a widened spinal canal and outwardly displaced neural arches (Barnes, 1994). Cleft neural arches would then be characterized as affecting one or two vertebral segments and presenting with a normal sacral canal and neural arches that are not pushed outwards (Barnes, 1994). Kumar and Tubbs (2011) rejected the description of SBO with NTD offered by Barnes as other pathologies (e.g., intradural lipomas, dermal sinus tracts) also present with a widened sacral canal.

Spina bifida occulta usually affects the fifth lumbar vertebra (L5), the first sacral segment (S1), or the second sacral (S2) segments (Nutter, 1913; Fidas *et al*., 1987; Saluja, 1988; Barnes, 1994; Simalcsik *et al*., 2011; Tamas-Csab *et al*., 2019). Some studies recorded spina bifida occulta along the entire sacrum. This included cases where the sacrum was open at the levels between S3 and S5 (Albrecht, 2007; Singh, 2013; Groza *et al*., 2016). SBO should not be mistaken for a sacral hiatus, which often occurs on S4 and S5, and represents normal anatomical variation (Nagar, 2004; Roberts and Manchester, 2005; Moore *et al*., 2014). According to Kumar and Tubbs (2011), although all open sacral segments should be noted, an open S3-S5 is usually regarded as a normal variation of the sacral hiatus.

Spina bifida terminology and assessment are not consistent among researchers. Most studies use the terms spina bifida or spina bifida occulta (Shore, 1930; Berry, 1975; Saluja, 1988; Jankauskas, 2001; Eubanks and Cheruvu, 2009). For the purpose of this research, the term spina bifida occulta will be used to indicate the incomplete union of the posterior neural arch or spinous processes in the thoraco-lumbo-sacral vertebra (Roberts and Manchester, 2005). In the thoraco-lumbar region, SBO was identified by an incomplete union of the posterior neural arch. In the sacrum, spina bifida occulta was assessed cranio-caudally from the first and second sacral segments onwards to rule out the normal anatomical variation of sacral hiatuses. In cases where only the neural arches of the fourth to the last sacral segments were not fused, the morphology is viewed as a sacral hiatus and not spina bifida occulta (Buikstra and Ubelaker, 1994; Kumar and Tubbs, 2011). Spina bifida occulta was classified as (1) complete, when all the sacral segments were affected (Buikstra and Ubelaker, 1994) and (2) incomplete, when vertebral segments above the fourth sacral segment were affected (Buikstra and Ubelaker, 1994) (Fig. 3.5). Lastly, the number of vertebral segments affected was also noted.

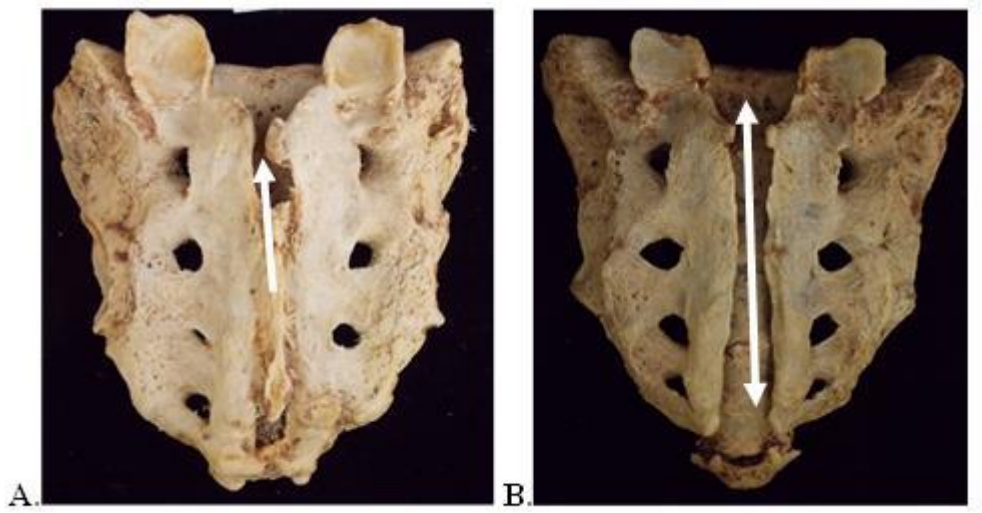


Figure 3.6: (A) Incomplete spina bifida with only two sacral segments affected (white arrow) (AN1411). (B) Complete spina bifida, with all sacral segments affected (white arrow). Posterior views (AN1430).

3.2.5 Spondylolysis

Spondylolysis can be identified by the separation of the vertebral body from the pars interarticularis or by a defect or partial separation of the pars interarticularis. An anomaly was classified as spondylolysis if a unilateral separation was observed, and as spondylolisthesis, if it occurred bilaterally (Buikstra and Ubelaker, 1994) (Fig. 3.6). Sidedness was noted in cases where the condition occurred unilaterally.

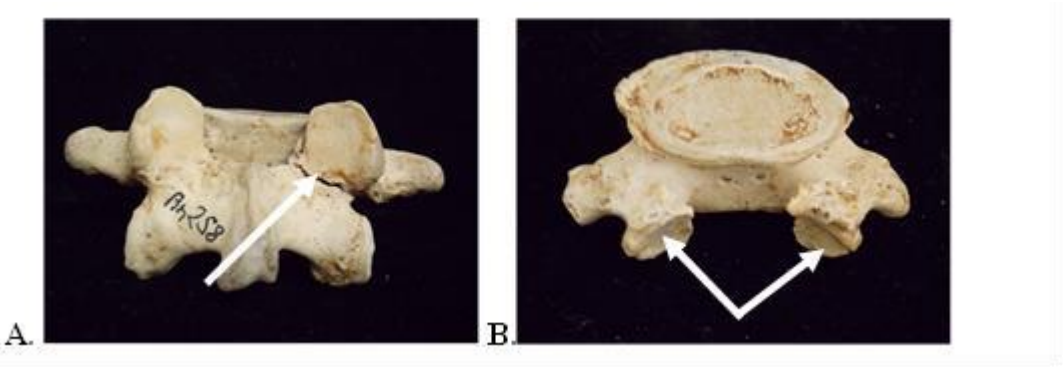


Figure 3.7: (A) Unilateral spondylolysis, arrow indicates an area of separation. Posterior view. (B). Spondylolisthesis, arrows indicate the bilateral separation. Inferio-posterior view (AN258).

3.2.6 Comorbidity conditions: Schmorl's nodes, vertebral compression, kyphosis and scoliosis

In addition to the developmental anomalies detailed above, other vertebral pathologies, including Schmorl's nodes, vertebral body compression, kyphosis and scoliosis, were noted as present or absent. Below the pathologies are briefly described:

Schmorl's nodes:

These are representations of the herniation of the nucleus pulposus through the cartilaginous end plate into the adjacent vertebral body (Peng *et al*., 20002; Williams *et al*., 2007). Schmorl's nodes may be asymptomatic but may be sometimes associated with low back pain

(Williams *et al*., 2007; Kyere *et al*., 2012). Schmorl's nodes were noted as present when a depression with sclerotic margins appeared on the vertebral body superior or inferior surface (Dar *et al*., 2009: E312) (Figure 3.8).

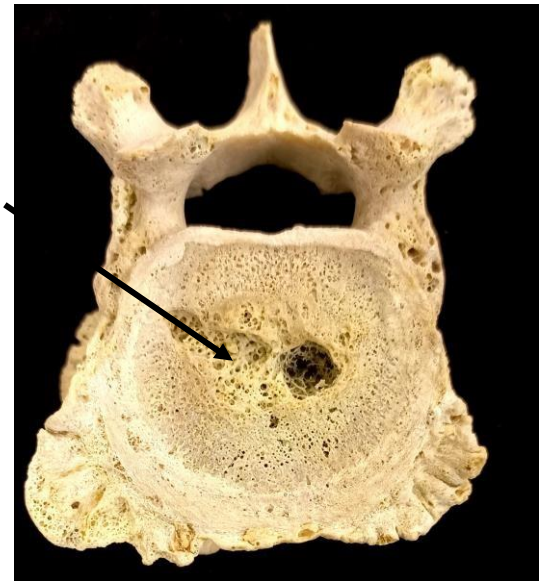


Figure 3.8: Schmorl's node on the superior vertebral body surface of T12 (A2461).

Vertebral body compression

Vertebral compression are usually due to osteoporosis but may sometimes be due to an overload of weight due the compromised biomechanics of the spine (Kutsal and Ergani, 2021). The biomechanics of the spine may be compromised by trauma or by the presence of developmental anomaly along the vertebral column. Vertebral compression was identified by collapsed, reduced vertebral body height (Kutsal and Ergani, 2021) (Figure 3.9).

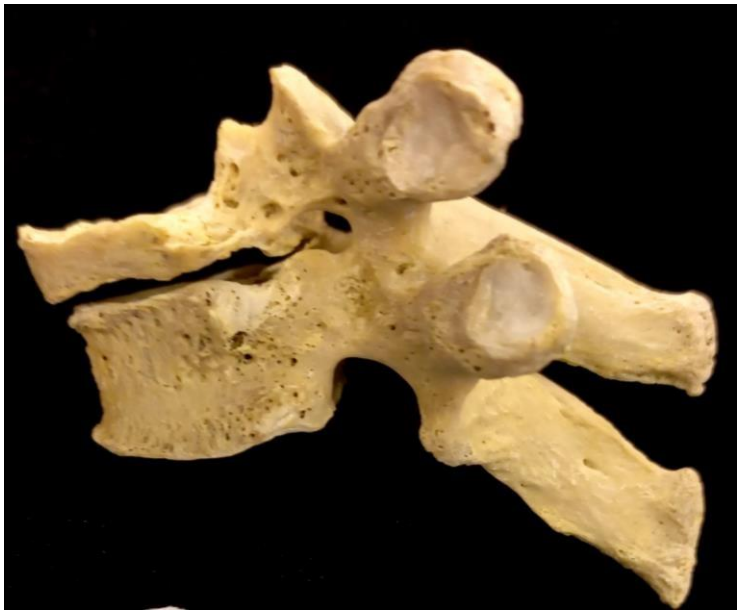


Figure 3.9: Vertebral body compression of T3. Lateral view (A2416).

Kyphosis

Kyphosis can be defined as an abnormal curvature (convex posteriorly) of the spine at the thoracic region, which produces a hunchback (Drake *et al*., 2015:76). The aetiology of kyphosis may include, trauma, developmental anomalies, and degenerative disc disease among others (Yaman and Dalbayrak, 2013). Kyphosis was identified by an articulated vertebral column that was convex posteriorly (Figure 3.10).

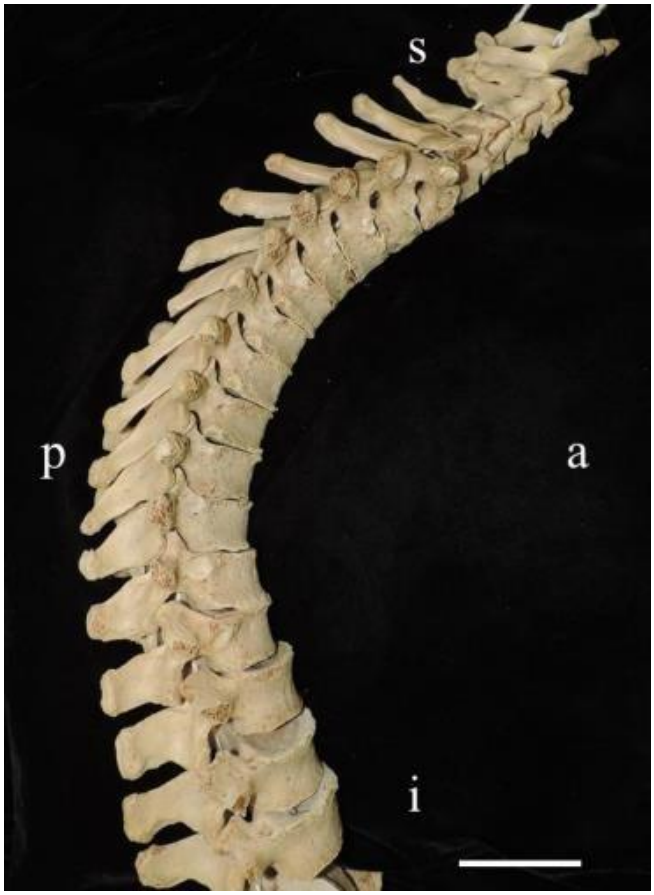


Figure 3.10: Kyphosis. a=anterior, p=posterior, s=superior, i=inferior (taken from Walters, 2016:70).

Scoliosis

Scoliosis can be defined as the abnormal lateral curvature of the spine (Drake *et al*., 2015:75). This condition may be developmental (congenital) or form secondary to the manifestation of certain developmental anomalies (relevant to this study) such as hemi-vertebra or sacralisation (Barnes, 2012b; Can, 2020). Scoliosis was noted as present when there was a lateral curvature of the articulated vertebral column.

3.3 Statistical analyses

Inter- and intra-observer repeatability of ordinal scores were determined for a subsample of 25 individuals randomly selected from the original sample. Scoring was done blind by the principal observer several months after the initial data collection, as well as by an independent observer. A weighted Cohen's kappa statistic was used to assess the repeatability of the classification system for the non-parametric data. A kappa value of less than 0.2 indicated poor agreement, whereas 0.21-0.4 was regarded as fair agreement, 0.41-0.6 indicated moderate agreement and 0.61-0.8 showed good agreement. Lastly, a value of 0.81-1.0 indicated very good agreement (Altman, 1991).

Data were analysed using descriptive statistics and frequency tables to present the variation of the observed developmental anomalies and pathologies in the total sample, between the sexes and among the population groups. Chi-squared tests of independence were used to determine significant differences in the frequency of anomalies between males and females, and among the three population groups of interest. A Yates continuity correction was used to compensate for the over-estimation of the Chi-square value when used for a 2 by 2 table (Pallant, 2011).

An alpha value of 0.05 or less was considered as significant (Pallant, 2011). A Fisher's exact test was used in cases where the expected frequency was less than 5 (Pallant, 2011).

The statistical programmes used to analyse the data were IBM SPSS v24, MedCalc v19.1.3, Social Science Statistics (www.socscistatistics.com) and Microsoft Excel 2016.

3.4 Ethical clearance

Ethical clearance was obtained from the School of Anatomical Sciences under the waiver granted for research on human skeletal materials in the school collections, with ethics number W-CJ-140604-1.

Chapter 4

RESULTS

4.1 Intra- and inter-observer repeatability analysis

A total of twenty-five individuals were re-assessed to determine the repeatability of the scoring method. This was done using the weighted Cohen's kappa test (Table 4.1). Results indicated kappa values for both intra- and inter-observer scores greater than 0.75, indicating excellent agreement (Fleiss, 2003). This shows that the scoring procedure used for the developmental anomalies in this study was sound and could be repeated with ease.

The random selection of the observer error sample resulted in none of the individuals in this subsample presenting with lumbarisation or supernumerary vertebrae. Those that were represented in the subsample are indicated in Table 4.1.

Table 4.1 Intra- and inter-observer repeatability results.

Developmental anomaly	**Intra-observer kappa**	**Inter-observer kappa**
Sacralisation	1.00	1.00
Spina bifida occulta	0.847	0.847
Spondylolysis	1.00	1.00
Sixth lumbar vertebra	1.00	1.00

4.2 General prevalence of vertebral developmental anomalies in the study sample

4.2.1 Total sample

Assessment of the combined sample of the three population subgroups provided general information about developmental anomalies in a South African sample. Of the total sample (*n*=902) assessed in this study, 22% (*n*=198) of the individuals presented with some form of developmental anomaly (Table 4.3). The majority of these anomalies were observed in males (66.7%, *n*=132) rather than in females (33.3%, *n*=66) and a Chi-squared test of independence with Yates correction indicated this difference to be statistically significant (χ^2= 44, *p*=0.00001). Furthermore, the SAB sample (38.4%, *n*=76) presented with more anomalies than the SAC (32.3%, *n*=64) or SAW (29.3%, *n*=58) samples. These differences were, however, not

statistically significant (SAB and SAC: χ^2=0.0396, *p*=0.8422; SAB and SAW: χ^2=0.8824, *p*=0.3475; SAC and SAW: χ^2=0.3814, *p*=0.5388).

The most prevalent anomaly in the sample was sacralisation 5.7% and the least prevalent was lumbarisation (1.9%) (Table 4.3). The order of developmental anomalies from most to least prevalent in the overall sample was sacralisation at 5.7%, spina bifida and spondylolysis each at 4.5%, L6 at 3.1%, T13 at 2.2% and lumbarisation at 1.9% (Table 4.3).

4.2.2 Male and female differences in the total sample

In the combined male sample (*n*=538), the order of developmental anomalies from most to least prevalent was as follows: sacralisation at 5.8%, spondylolysis at 5.6%, spina bifida occulta at 5%, L6 at 3.5%, lumbarisation at 2.4% and T13 at 2.2% (Table 4.3). For the females (*n*=364), the order was different with sacralisation at 5.5%, spina bifida occulta at 3.8%, spondylolysis at 3%, L6 at 2.5%, T13 at 2.2% and lumbarisation at 1.1% as the least frequent condition (Table 4.3). Males presented with the highest prevalence for all developmental anomalies, except for T13 where the male and female prevalence was equal. There was no statistically significant difference between the male and female prevalences for any of the individual developmental anomalies in the overall sample (Table 4.2).

Table 4.2 Chi-squared and Fisher's exact tests of significant differences between sexes of the total sample

Developmental anomaly	**Combined sample (Males vs. females)**
Sacralisation	χ^2 =0.021 *p*-value=0.885
Lumbarisation	*p*-value=1.000*
T13	*p*-value=0.616*
L6	*p*-value=0.759*
Spina bifida occulta	*p*-value=1.000*
Spondylolysis	*p*-value=0.148*

*Fisher's exact test.

4.2.3 Population differences

The following developmental anomalies were more common in the SAB than the SAC or SAW samples: sacralisation at 7.7% (*n*=25); spina bifida occulta at 5.2% (*n*=17) and supernumerary 13th thoracic vertebra at 2.8% (*n*=9) (Table 4.3). Sacralisation was the only anomaly that showed statistically significant difference between SAB and SAW (χ^2=7.6729, *p*= 0.0056) and between SAC and SAW (χ^2=5.0755, *p*= 0.0244). The difference between sacralisation prevalences between SAB and SAC was not statistically significant (χ^2=0.1181, *p*= 0.7311).

Supernumerary sixth lumbar vertebra (4.2%; *n*=12) was more common in the SAC sample, but these differences were however not statistically significant (with Yates correction) (SAB and SAC: χ^2=0.2737, *p*=0.6009; SAB and SAW: χ^2=0.2884, *p*=0.5912; SAC and SAW: χ^2=1.5246, *p*=0.2169). Moreover, lumbarisation (2.7%; *n*=8) and spondylolysis (5.5%; *n*=16) were more common in the SAW sample (Table 4.3). For lumbarisation, all the prevalence differences between the three population groups were not statistically significant (SAB and SAC: Fisher's exact test value=0.3171, *p*>0.05); SAB and SAW: Fisher's exact test value =0.1266, *p*>0.05; SAC and SAW: Fisher's exact test value= 0.5903, *p*>0.05). For Spondylolysis, the differences observed between the three population groups were also not statistically significant (SAB and SAC: χ^2=0.1066, *p*= 0.7440); SAB and SAW: χ^2=0.7754, *p*=0.3786; SAC and SAW: χ^2= 0.111, *p*=0.7390).

For the SAB sample, sacralisation (7.7%) was the most prevalent anomaly whereas lumbarisation (0.9%) was the least. Similar to the SAB sample, sacralisation (6.6%) was the most common anomaly in the SAC sample, whereas the 13th thoracic vertebra (1.4%) was the least common (Table 4.3). Lastly, the SAW sample had spondylolysis presenting with the highest prevalence at 5.5% while the sixth lumbar vertebra (2.1%) was the least prevalent (Table 4.3).

4.2.4 Sex differences within each population

South African Black sample

Sacralisation

The total prevalence of sacralisation within the Black South African sample (*n*=325) was 7.7% (*n*=25) (Table 4.3). The prevalence for males was at 7.6% (*n*=14) and for females at 7.9 % (*n*=11). The higher prevalence observed in females was due to the smaller sample the larger male sample size. A Chi-squared test of independence with Yates correction indicated no statistical significance for the male and female difference (χ^2=0.009, *p*=0.923).

Lumbarisation

The SAB sample presented an overall prevalence of 0.9% (*n*=3). This prevalence was observed only in males.

13th thoracic vertebra

The overall prevalence for the 13th thoracic vertebra within the Black South African sample was 2.8% (*n*=9). Males had a 3.2% (*n*=6), and females had a 2.1% *(n*=3), prevalence. The difference in prevalence for the 13th thoracic vertebra between the South African males and females was not statistically significant (Fisher's exact test: *p*=0.737).

Sixth lumbar vertebra

The Black South African sample had an overall 3.1% (*n*=10) prevalence for the sixth lumbar vertebra. The male sample had a higher prevalence of 3.8% (*n*=7) compared to their female counterparts at 2.1% (*n*=3). The difference in prevalence for the sixth lumbar vertebra between males and females in the SAB sample was not statistically significant (Fisher's exact test: *p*=0.759).

Spina bifida occulta

The overall prevalence within the Black South African sample was 5.2% (*n*=17), where a higher prevalence was seen in the male sample at 5.9% (*n*=11) compared to females at 4.3%, (*n*=6) (Table 4.3). Differences between males and females with regards to spina bifida were, however, not statistically significant (χ^2=0.443, *p*=0.506).

Spondylolysis

The overall prevalence of spondylolysis within the Black South African sample was 3.7% (*n*=12) (Table 4.3). Males presented with a higher 4.3% (*n*=8) prevalence, compared to 2.9% (*n*=4) in females. A Chi-squared test for independence with Yates correction indicated no significant difference between the male and female prevalences (χ^2=0.482, *p*=0.487).

South African Coloured (SAC) sample

Sacralisation

The overall prevalence of sacralisation within the SAC sample was 6.6% (*n*=19) (Table 4.3).

Males in the SAC sample presented a prevalence of 6.5% (*n*=12) and females with a 6.9% (*n*=7) prevalence (Table 4.3). The difference between males and females was not statistically significant (Fisher's exact test: p-value=0.603, *p*>0.05).

Lumbarisation

The overall prevalence of lumbarisation within the SAC sample was 2.1% (*n*=6). South African males had a higher prevalence of 2.2% (*n*=4) and females a lower 0.7% (*n*=2). Statistical significance difference was not calculated due to the small sample size.

13th Thoracic vertebra

The SAC sample had a 1.4% (*n*=4) 13th thoracic vertebra prevalence, where males had 1.1% *n*=2) and females 2% (*n*=2) prevalence. Although the prevalence differs due to the difference in sample sizes, the actual number of males and females presenting with the 13th thoracic vertebra is equal.

Sixth lumbar vertebra

The overall prevalence for the sixth lumbar vertebra within the SAC sample was 4.2% (*n*=12). Females presented with a higher prevalence 5% (*n*=5) and males a lower 3.8% (*n*=7). This difference was, however, not statistically significant (Fisher's exact test value=0.759, *p*>0.05).

Spina bifida occulta

With regards to spina bifida occulta, an overall prevalence of 3.5% (*n*=10) was seen within the SAC sample (Table 4.3). Males had a higher 3.8% (*n*=7) and females a lower 3% (*n*=3) prevalence (Table 4.3). There was no statistical significance for the difference in prevalence between males and females (Fisher's exact test value=1.000, *p*>0.05).

Spondylolysis

The overall prevalence of spondylolysis within the SAC sample was 4.5% (*n*=13) (Table 4.3). Males presented with a prevalence of 5.9% (*n*=11) and females with a lower prevalence of 2% (*n*=2) (Table 4.3). Statistical significance difference was not calculated due to the small sample size.

South African White (SAW) sample

Sacralisation

The overall prevalence of sacralisation within the SAW sample was 2.4% (*n*=7), this prevalence was higher in males at 3% (*n*=5) and lower in females at 1.6% (*n*=2) (Table 4.3).

Statistical significance difference was not calculated due to the small sample size.

Lumbarisation

With regards to lumbarisation, there was an overall prevalence of 2.7% (*n*=8) within the SAW sample (Table 4.3). Males had a higher prevalence of 3.6% (*n*=6) than females at 1.6% *(n*=2) (Table 4.3). Statistical significance difference was not calculated due to the small sample size.

13th Thoracic vertebra

The SAW sample had an overall prevalence of 2.4% (*n*=7) for the 13th thoracic vertebra. The male (2.4%, *n*=4) and female (2.4%, *n*=3) prevalences were equal, however, the number of males was slightly higher than that of females. Statistical significance difference was not calculated due to the small sample size.

Sixth lumbar vertebra

An overall prevalence of 2.1% (*n*=6) for the sixth lumbar vertebra was seen in the SAW sample. Males had a higher prevalence of 3% (*n*=5) and females had only 0.8% *(n*=1).

Statistical significance difference was not calculated due to the small sample size.

Spina bifida occulta

The overall prevalence for spina bifida occulta within the SAW sample was 4.8% (*n*=14) (Table 4.3). Males had a higher prevalence of 5.4% (*n*=9) and females had 4.1% (*n*=5) (Table 4.3). The difference between males and females was not statistically significant (χ^2 =0.259, *p*=0.611).

Spondylolysis

The overall prevalence of spondylolysis within the SAW sample was 5.5% (*n*=16) (Table 4.3). Males had a higher total prevalence of 6.5% (*n*=11) than females (4.1%, *n*=5) (Table

4.3). Male and female differences were not statistically significant (χ^2 =0.842, *p*=0.359).

Table 4.3 Prevalence of developmental anomalies in the study sample.

		Sacralisation	**Lumbarisation**	**T13**	**L6**	**Spina bifida occulta**	**Spondylolysis**
SAB (n=325)	Males (n=185)	7.6% (*n*=14)	1.6% (*n*=3)	3.2% (*n*=6)	3.8% (*n*=7)	5.9% (*n*=11)	4.3% (*n*=8)
	Females (n=140)	7.9% (*n*=11)	0	2.1% (*n*=3)	2.1% (*n*=3)	4.3% (*n*=6)	2.9% (*n*=4)
Total	**325**	**7.7% (*n*=25)**	**0.9% (*n*=3)**	**2.8% (*n*=9)**	**3.1% (*n*=10)**	**5.2% (*n*=17)**	**3.7% (*n*=12)**
SAC (n=286)	Males (*n*=185)	6.5% (*n*=12)	2.2% (*n*=4)	1.1% (*n*=2)	3.8% (*n*=7)	3.8% (*n*=7)	5.9% (*n*=11)
	Females (*n*=101)	6.9% (*n*=7)	2% (*n*=2)	2% (*n*=2)	5% (*n*=5)	3% (*n*=3)	2% (*n*=2)
Total	**286**	**6.6% (*n*=19)**	**2.1% (*n*=6)**	**1.4% (*n*=4)**	**4.2% (*n*=12)**	**3.5% (*n*=10)**	**4.5% (*n*=13)**
SAW (n=291)	Males (*n*=168)	3% (*n*=5)	3.6% (*n*=6)	2.4% (*n*=4)	3% (*n*=5)	5.4% (*n*=9)	6.5% (*n*=11)
	Females (*n*=123)	1.6% (*n*=2)	1.6% (*n*=2)	2.4% (*n*=3)	0.8% (*n*=1)	4.1% (*n*=5)	4.1% (*n*=5)
Total	**291**	**2.4% (*n*=7)**	**2.7% (*n*=8)**	**2.4% (*n*=7)**	**2.1% (*n*=6)**	**4.8% (*n*=14)**	**5.5% (*n*=16)**
Combined (n=902)	Males (*n*=538)	5.8% (*n*=31)	2.4% (*n*=13)	2.2% (*n*=12)	3.5% (*n*=19)	5.% (*n*=27)	5.6% (*n*=30)
	Females (*n*=364)	5.5% (*n*=20)	1.1% (*n*=4)	2.2% (*n*=8)	2.5% (*n*=9)	3.8% (*n*=14)	3.0% (*n*=11)
TOTAL	**902**	**5.7% (*n*=51)**	**1.9% (*n*=17)**	**2.2% (*n*=20)**	**3.1% (*n*=28)**	**4.5% (*n*=41)**	**4.5% (*n*=41)**

*Percentages based on the actual number of individuals observed. All percentages are rounded to the nearest decimal place.

4.2.5 The prevalence of multiple developmental anomalies and spinal pathologies within the study sample

Total sample

Of the 198 individuals who presented with some form of developmental anomaly in the overall sample, 6.7% (*n*=13) of the cases either presented with multiple anomalies and/or some form of spinal pathology. A higher prevalence for multiple anomalies and/or spinal pathology was seen in males (61.5%, *n*=8) rather than in females (38.5%, *n*=5) of the total sample. Most individuals presented with multiple anomalies (69.2%, *n*=9) and most were males 55.6% (*n*=5) compared to the female counterparts 44.4% (*n*=4).

Four of the nine individuals who presented with multiple anomalies also presented with some form of spinal pathology (44.4%) in the total sample. The majority of these individuals were males (75%, *n*=3) while the minority was females (25%, *n*=1).

Four (30.8%) of the remaining 13 cases presented with a single type of developmental anomaly. The majority of the cases were accompanied by a single spinal pathology (75%, *n*=3), and one individual had a single anomaly plus two spinal pathologies (25%, *n*=1).

Population differences

The SAB population presented with a slightly higher prevalence for multiple anomalies (44.4%, *n*=4) followed by the SAW (33.3%, *n*=3) and the SAC (22.2%, *n*=2). In addition, the prevalence of cases with multiple anomalies accompanied by a form of spinal pathology was seen in SAB (50%, *n*=2), followed by SAC and SAW who had equal representations at 25% (*n*=1) each.

There were slightly more SAW (66.7%, *n*=2) than SAW (33.3%, *n*=1) individuals who presented with a single anomaly accompanied by one form of spinal pathology. SAC were not observed for this grouping. The remaining 1 case presented with 1 anomaly and 2 forms of pathologies.

There was a lot of variation in the representation of multiple developmental anomalies, or a developmental anomaly accompanied by a spinal pathology. Below, a few cases with similar representation are discussed:

1. A combination of sacralisation and block vertebra was observed in three individuals. The vertebral segments affected in the block vertebra were however not consistent. Two of these

cases were bilateral occurrences (Types II and III) and one was a unilateral occurrence (Type IA).

2. Three of the four bilateral spondylolysis cases presented with vertebral body compression, two of the spondylolysis cases occurred on L5 and the other one on L2. Nonetheless, the vertebral level of the compressed vertebral segments was not consistent even for the 2 cases with spondylolysis at L5.

Below are the descriptions of each case that presented with multiple anomalies and/ or spinal pathology:

- **Case 1 (AN1295)**: A 52-year-old SAC female presented with bilateral sacralisation (Type II) with a pseudo-facet on the right side. This individual also presented with spina bifida occulta (Type 1) on T1. In addition, block vertebra was observed from T1-T4.

- **Case 2 (A2050)**: A 67-year-old SAW male with bilateral sacralisation (Type III) had an anterior fusion of the T12 and L1 bodies (block vertebra).

- **Case 3 (A203)**: A 40-year-old SAB male presented with bilateral sacralisation (Type IB) on L5, and bilateral spondylolysis (Type 2) on L4. Schmorl's nodes were observed on the superior vertebral body of T6 and on the inferior surface of T7.

- **Case 4 (1847)**: A 79-year-old SAW female presented with unilateral sacralisation (Type IA) with a pseudo-facet/arthrosis. The vertebral bodies and spinous processes of T4 and T5 were fused (block vertebrae).

- **Case 5 (1703)**: A 77-year-old SAW female presented with unilateral lumbarisation (Type I) and fusion of the vertebral bodies and spinous processes of T6 and T7. A vertebral body compression fracture was observed on T11.

- **Case 6 (A2461)**: A 66-year-old SAW male presented with bilateral lumbarisation (Type IB) and Schmorl's nodes on T6-T12.

- **Case 7 (A1879)**: A 65-year-old SAB female presented with a supernumerary T13 and unilateral left sacralisation with a pseudo-facet/arthrosis. There was a presence of bilateral 13th ribs. On the left, the rib was fused to the T13.

- **Case 8 (A3575)**: An 87-year-old SAW male presented with SBO at S1-S2. The vertebral bodies of T6 and T7 were compressed and the vertebral column was kyphotic (hunched back).

- **Case 9 (A1314)**: A 34-year-old SAB male presented with SBO (Type 2). The inferior articulating facets of T2 were fused with the superior articulating facets of T3.
- **Case 10 (A2176)**: A 49-year-old SAW male presented with bilateral spondylolysis (Type 2) on L5. Schmorl's nodes were present on the vertebral bodies of T7 through L2.

- **Case 11 (A2416)**: A 67-year-old SAC male presented with bilateral spondylolysis (Type 2) on L5. T3 and T4 were fused at the inferior and superior articulating facets and the T3 vertebral body appeared greatly compressed.

- **Case 12 (A3592)**: A 55-year-old SAB male presented with bilateral spondylolysis (Type 2) on L5. The vertebral body of L5 was compressed.

- **Case 13 (A3721)**: A 60-year-old SAB male presented with bilateral spondylolysis (Type 2) on L2 and SBO (Type 1) on S1. Vertebral body compression was observed on L2 and L3.

4.3 Prevalence of developmental anomalies' subtypes in the total sample and in the total male and female samples

The following developmental anomalies could be further classified according to type and prevalence. Results of each will be reported in this section.

Sacralisation

In the total sample, Type I (70.1%, *n*=38) was more prevalent than Types II (11.8%, *n*=6) or III (13.7%, *n*=7) (Table 4.4). Statistically significant differences were only observed between Types I and II (χ^2 =38.4099, p<0.00001) and Types I and III (χ^2 =35.7895, p<0.00001). In addition, a bilateral occurrence was more prevalent than a unilateral occurrence and in cases where there was a unilateral occurrence, the left side was more prevalent at 27.5% (*n*=14) (Table 4.4).

Table 4.4 Prevalence of sacralisation types for the total sample.

Sacralisation type	**ɨidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I (*n*=38)	34.2% (*n*=13)	26.3% (*n*=10)	39.5% (*n*=15)
II (*n*=6)	16.7% (*n*=1)	0	83.3% (*n*=6)
III (*n*=7)	0	0	100% (*n*=7)
TOTAL (*n*=51)	27.5% (*n*=14)	19.6% (*n*=10)	54.9% (*n*=28)

All percentages are rounded to the nearest decimal place.

For males, Type I (64.5%; *n*=20) sacralisation was more prevalent than Types II and III (Table 4.5). This difference was statistically significant (χ^2 =13.8795, *p*=0.0001). In general, a bilateral occurrence (58.1%; *n*= 18) was more common and in cases of unilateral occurrences, the left side (29%; *n*= 9) was more prevalent than the right side (12.9%; *n*= 4) (Table 4.5). For the Type 1 sacralisation cases in males, a unilateral left occurrence was more prevalent than the bilateral or right occurrences (Table 4.5). Like males, females also had a higher prevalence of Type 1 sacralisation (90%; *n*= 18) (Table 4.6), however, a unilateral right occurrence was slightly more prevalent than a unilateral left occurrence (Table 4.6).

Table 4.5 Prevalence of sacralisation types for the total male sample.

Sacralisation type	**ɨidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 64.5% (*n*=20)	45% (*n*=9)	20% (*n*=4)	35% (*n*=7)
II- 16.1%(*n*=5)	0	0	100% (*n*=5)
III- 19.4% (*n*=6)	0	0	100% (*n*=6)
TOTAL (*n*=31)	29% (*n*=9)	12.9% (*n*=4)	58.1% (*n*=18)

All percentages are rounded to the nearest decimal place.

Table 4.6 Prevalence of sacralisation types for the total female sample.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 90% (*n*=18)	22.2% (*n*=4)	33.3% (*n*=6)	44.4% (*n*=8)
II- 5% (*n*=1)	0.1% (*n*=1)	0	0
III- 5% (*n*=1)	0	0	0.1% (*n*=1)
TOTAL (*n*=20)	25% (*n*=5)	30% (*n*=6)	45% (*n*=9)

All percentages are rounded to the nearest decimal place.

Lumbarisation

In the total sample, Type I (64.7%, *n*=11) was more prevalent than Type II (35.3%, *n*=6) (Table 4.7). This difference was, however, not statistically significant (χ^2 =2.9412, *p*=0.0863). In general, a unilateral occurrence was more common than a bilateral occurrence. A bilateral occurrence (41.2%) was, however, more common than the unilateral left or right occurrences, each at 29.4% (Table 4.7).

Table 4.7 Prevalence of lumbarisation types for the total sample.

Lumbarisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 64.7% (*n*=11)	45.5% (*n*=5)	45.5% (*n*=5)	9.1% (*n*=1)
II- 35.3% (*n*=6)	0	0	100% (*n*=6)
TOTAL (*n*=17)	29.4% (*n*=5)	29.4% (*n*=5)	41.2% (*n*=7)

For males, Type 1 (69.2%; *n*= 9) was more frequent than Type II (30.8%; *n*= 4) and this difference was not statistically significant (Fisher's exact test: *p*=0.12). Females, on the other hand, had an equal representation for both types (Table 4.8). Moreover, in males, unilateral lumbarisation was slightly more prevalent than a bilateral occurrence, specifically a unilateral left occurrence (38.5%; *n*= 5) (Table 4.8). In females, a bilateral occurrence of lumbarisation (75%; *n*= 3) was slightly more prevalent than a unilateral occurrence (25%) (Table 4.9).

Table 4.8 Prevalence of lumbarisation types for the total male sample.

Lumbarisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 69.2% (*n*=9)	55.6% (*n*=5)	44.4% (*n*=4)	0
II- 30.8% (*n*=4)	0	0	100% (*n*=4)
TOTAL (*n*=13)	38.5% (*n*=5)	30.8% (*n*=4)	30.8% (*n*=4)

All percentages are rounded to the nearest decimal place.

Table 4.9 Prevalence of lumbarisation types for the total female sample.

Lumbarisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 50% (*n*=2)	0	50% (*n*=1)	50% (*n*=1)
II- 50% (*n*=2)	0	0	100% (*n*=2)
TOTAL (*n*=4)	0	25% (*n*=1)	75% (*n*=3)

All percentages are rounded to the nearest decimal place.

Spina bifida occulta

Males presented with both types of spina bifida occulta; Type 1 was more prevalent 88.9% (*n*=24) than Type 2 11.1% (*n*=3) and this difference was statistically significant (Fisher's exact test value is < 0.00001, $p<0.05$). All 14 affected females presented with spina bifida occulta Type 1.

Spina bifida occulta was observed throughout the thoraco-lumbo-sacral region of the sample. Overall, it occurred more frequently in the sacral region (70.4%, *n*=19), especially on S1 (Table 4.10). The least affected was the lumbar region. In the thoracic region, it occurred more frequently on the first thoracic vertebra (T1) followed by T11 (Table 4.10). In the lumbar region, it was more frequent on L5 (Table 4.10).

In the overall male sample, the sacral region was the most affected, whereas, in females, the thoracic region was more affected, specifically T11 (Table 4.10).

Table 4.10 Spina bifida occulta type and the specific vertebrae affected by SBO in the total male and female samples.

Total male sample		**Total female sample**	
SBO type	Vertebra affected	SBO type	Vertebra affected
1	(2) T1	1	T1
1	T1-T2	1	T1 & T3
1	T1-T2 & L1	1	T5
1	T11	1	T10
1	T11 & S1	1	T11- L1
1	L5	1	T12- L1
1	L4-L5	1	T11
1	(5) S1	1	T11-T12
1	(11) S1-S2	1	L4-S2
2	(3) S1-S5	1	(2) L5
		1	S1
		1	(2) S1-S2

Spondylolysis

In the total sample, Type 2 (82.9%) spondylolysis was more prevalent than Type 1 (17.1%) and this difference was statistically significant ($\chi^2 = 35.561$, $p < 0.00001$). A bilateral occurrence (82.9%) was generally more common in the overall sample (Table 4.11). Furthermore, a unilateral left (14.6%) occurrence was more common than a right (2.4%) occurrence (Table 4.11).

Table 4.11 Prevalence of spondylolysis types for the total sample.

Spondylolysis type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
1- 17.1% (*n*=7)	85.7% (*n*=6)	14.3% (*n*=1)	0
2- 82.9% (*n*=34)	0	0	100% (*n*=34)
TOTAL (*n*=41)	14.6% (*n*=6)	2.4% (*n*=1)	82.9% (*n*=34)

All percentages are rounded to the nearest decimal place.

A bilateral, Type 2 presentation (76.7%) was more common for males than a unilateral occurrence of Type 1 (23.3%) spondylolysis (Table 4.12) and this difference was statistically significant (χ^2 = 17.0667, *p*= 0.000036). In cases of unilateral spondylolysis, the left (85.7%) occurrence was more common than the right (14.3%) (Table 4.12). Females, on the other hand, presented with spondylolysis Type 2 only, with all bilateral occurrences.

Table 4.12 Prevalence of spondylolysis types for the total male sample.

Spondylolysis type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
1- 23.3% (*n*=7)	85.7% (*n*=6)	14.3% (*n*=1)	0
2- 76.7% (*n*=23)	0	0	100% (*n*=23)
TOTAL (*n*=30)	20% (*n*=6)	3.3% (*n*=1)	76.7% (*n*=23)

All percentages are rounded to the nearest decimal place.

Spondylolysis was localised between L2-L5 in the overall and the male sample (Table 4.13). In the female sample, it was localised between L3-L5 (Table 4.13). The most affected vertebra was L5 in the overall (75.6% *n*=31) and the male and female subsamples, even within the different spondylolysis types. (Table 4.13).

Three individuals presented with multiple spondylolysis: a 70-year-old SAB female, and a 45year-old SAC male both presented with bilateral spondylolysis (Type 2) on L4 and L5 (Table 4.13). A 73-year-old SAW male presented with bilateral spondylolysis (Type 2) from L3-L5 (Table 4.13).

Table 4.13 Occurrence, vertebra affected, and age of individuals affected by spondylolysis in the South African sample.

Males		**Females**	
Occurrence (unilateral or bilateral)	Vertebral level affected	Occurrence (unilateral or bilateral)	Vertebral level affected
1	L2 (*n*=2)	2	L3
1	L3 (*n*=2)	2	L4
1	L5 (*n*=5)	2	L5 (*n*=8)
2	L2	2	L4 & L5
2	L4 & L5		
2	L3-L5		

*1= Unilateral occurrence (Type 1) *2= Bilateral occurrence (Type 2)

4.4 Prevalence of the developmental anomalies' subtypes in and within each subsample

South African Black sample

Sacralisation

In the overall SAB sample, Type I (76%) was more prevalent than other types (Table 4.14). In general, a bilateral occurrence (60%) was the most common and in unilateral cases, the left (24%) was slightly more common than the right (16%) (Table 4.14). For type 1, a bilateral was more common than a unilateral left or right occurrence (Table 4.14).

Table 4.14 Prevalence of sacralisation types in the total South African Black sample.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 76% (*n*=19)	31.6% (*n*=6)	21.1% (*n*=4)	47.4% (*n*=9)
II- 12% (*n*=3)	0	0	100% (*n*=3)
III- 12% (*n*=3)	0	0	100% (*n*=3)
TOTAL 100% (*n*=25)	24% (*n*=6)	16% (*n*=4)	60% (*n*=15)

For males, Type I (57.1%) was more prevalent than other type with the expressions evenly split in terms of side (Table 4.15). Females presented with Type I sacralisation only, with unilateral right sides (27.3%, *n*=3) being slightly more common than the left (18.2%, *n*=2) (Table 4.16). The bilateral occurrence was more common among the sacralisation cases in both the male and

female samples (Tables 4.15 and 4.16). Moreover, the prevalence of sacralisation Type I was higher in females (100%) (Table 4.16) than in males (57.1%) (Table 4.15).

Table 4.15 Prevalence of sacralisation types in South African Black males.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 57.1% (*n*=8)	50% (*n*=4)	12.5% (*n*=1)	37.5% (*n*=3)
II- 21.4% (*n*=3)	0	0	100% (*n*=3)
III- 21.4% (*n*=3)	0	0	100% (*n*=3)
TOTAL 100% (*n*=14)	28.6% (*n*=4)	7.1% (*n*=1)	64.3% (*n*=9)

All percentages are rounded to the nearest decimal place.

Table 4.16 Prevalence of sacralisation types in South African Black females.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I (*n*=11)	18.2% (*n*=2)	27.3% (*n*=3)	54.5% (*n*=6)

Lumbarisation

Lumbarisation was only observed in males, therefore, both types were observed in this sample, with Type II (66.7%, *n*=2) being more prevalent.

Spina bifida occulta

Males presented with both types of spina bifida occulta, with Type 1 showing a higher prevalence (90.9%, *n*=10) compared to Type 2 (9.1%, *n*=1). Females only presented with Type 1 (*n*=6).

In the overall SAB sample, spina bifida occulta presented itself in the thoraco-lumbo-sacral region. The first thoracic vertebra (T1) was most affected in the thoracic region, in the overall and male samples (Table 4.17). In the lumbar region, L1 was commonly affected. The occurrence of SBO in the lumbar region was only observed in females (Table 4.17).

Furthermore, S1 was frequently affected in the overall and male samples.

The most affected vertebrae in the overall SAB sample were the first sacral segment (S1) followed by T1 (Table 4.17). In males, SBO was only seen in the thoracic and sacral regions and S1 was more commonly affected. In females, it was observed in the thoraco-lumbo-sacra regions and vertebral segments T12 and L1 were the most affected elements (Table 4. 17).

Table 4.17 Spina bifida occulta type and the specific vertebrae affected by SBO in the Black sample.

South African Black males		**South African Black females**	
SBO type	Vertebra affected	SBO type	Vertebra affected
1	T1	1	T1 & T3
1	T1-T2	1	T5
1	T1-T2 & L1	1	T10
1	T11	1	T11- L1
1	T11 & S1	1	T12- L1
1	(2) S1	1	L4-S2
1	(3) S1-S2		
2	S1-S5		

Spondylolysis

Both South African Black (SAB)males and females presented with Type 2 spondylolysis only. Table 4.18 shows the occurrence, of vertebra affected of SAB males and females affected by spondylolysis. In the male sample, four of the 8 cases occurred on L5, two of the cases occurred on L2 and only one case occurred on L4 and L5 respectively (Table 4.18). In the female sample, there were single representations of spondylolysis on L3, L4 and L5. In addition, a 70-year-old female presented with multiple levels of spondylolysis involving L4 and L5. All the cases in the SAB sample occurred bilaterally (Type 2) (Table 4.18).

Table 4.18 Spondylolysis in the South African Black sample.

South African Black males		**South Afriacn females**	
Occurrence (unilateral or bilateral)	Vertebral level affected	Occurrence (unilateral or bilateral)	Vertebral level affected
1	L3	2	L3
1	L5	2	L4
2	L2 (*n*=2)	2	L5
2	L3	2	L4 & L5
2	L4		
2	L5 (*n*=4)		

*2= Bilateral occurrence (Type 2)

South African Coloured (SAC) sample

Sacralisation

For the SAC sample, type I (73.7%) was more prevalent than Types II (15.8%) or III (10.5%) (Table 4.19). Significant differences were not tested due to the small sample for Type III. A bilateral occurrence (47.4%) was more common than a unilateral left (31.6%) or right (21.1%) occurrences (Table 4.19).

For Type I, the unilateral left and bilateral occurrences had equal representations with each at 35.7%. This was slightly more than the unilateral right prevalence (28.6%) (Table 4.19). For Type II, a bilateral occurrence was more common (66.7%) (Table 4.19).

Table 4.19 Prevalence of sacralisation types in the total South African Coloured sample.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 73.7% (*n*=14)	35.7% (*n*=5)	28.6% (*n*=4)	35.7% (*n*=5)
II- 15.8% (*n*=3)	33.3% (*n*=1)	0	66.7% (*n*=2)
III- 10.5% (*n*=2)	0	0	100% (*n*=2)
TOTAL (*n*=19)	31.6% (*n*=6)	21.1% (*n*=4)	47.4% (*n*=9)

South African Coloured males presented with all types of sacralisation although Type I was more prevalent (66.7%) (Table 4.20). In general, a bilateral occurrence was more commonly observed than a unilateral left and right occurrence in SAC males (Table 4.20). The sample for Types II and III, and for this reason, statistical significance was not tested.

Females presented with sacralisation Types I and II, where Type I (85.7%) was more prevalent (Table 4.21). The difference in prevalence for sacralisation between the males and females was not tested due to a small sample size. In addition, the unilateral right occurrence had a higher prevalence than the unilateral or bilateral occurrences in the females (Table 4.21).

Table 4.20 Prevalence of sacralisation types in South African Coloured males.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 66.7% (*n*=8)	50% (*n*=4)	12.5% (*n*=1)	37.5% (*n*=3)
II- 16.7% (*n*=2)	0	0	100% (*n*=2)
III-16.7% (*n*=2)	0	0	100% (*n*=2)
TOTAL (*n*=12)	33.3% (*n*=4)	8.3% (*n*=1)	58.3% (*n*=7)

All percentages are rounded to the nearest decimal place.

Table 4.21 Prevalence of sacralisation types in South African Coloured females.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I-85.7% (*n*=6)	16.7% (*n*=1)	50% (*n*=3)	33.3% (*n*=2)
II- 14.3% (*n*=1)	100% (*n*=1)	0	0
TOTAL (*n*=7)	28.6% (*n*=2)	42.9% (*n*=3)	28.6% (*n*=2)

All percentages are rounded to the nearest decimal place.

Lumbarisation

In the SAC sample, Type I and II had equal representations. Unilateral and bilateral occurrences were also represented equally (Table 4.22).

Table 4.22 Prevalence of lumbarisation types in the total South African Coloured sample.

Lumbarisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 50% (*n*=3)	100% (*n*=3)	0	0
II- 50% (*n*=3)	0	0	100% (*n*=3)
TOTAL (*n*=6)	75% (*n*=3)	0	25% (*n*=1)

The overall prevalence for lumbarisation within the SAC sample was 2.1% (*n*=6); SAC males had a slightly higher prevalence of 2.2% (*n*=4) (Table 4.23). Males in this sample presented with both lumbarisation types, whereas females presented with Type II (*n*=2) only. For males, Type I (75%) was more prevalent, presenting with a unilateral left occurrence only and for Type II, one individual presented with a bilateral occurrence (Table 4.23). A unilateral left was, therefore, more common in this sample. Statistical difference between the types in the SAC male sample was done due to the small sample size.

Table 4.23 Prevalence of lumbarisation types in South African Coloured males.

Lumbarisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I-75% (*n*=3)	100% (*n*=3)	0	0
II-25% (*n*=1)	0	0	100% (*n*=1)
TOTAL (*n*=4)	75% (*n*=3)	0	25% (*n*=1)

All percentages are rounded to the nearest decimal place

Spina bifida occulta

South African Coloured males presented with both spina bifida occulta types (Type 1 at 85.7 5, *n*=6 and Type 2 at 14.3%, *n*=1), whereas females only presented with Type 1. In the SAC males, SBO was observed in the thoracic, lumbar and sacral vertebra while the females only presented SBO in the thoracic region. SBO in the thoracic vertebrae was more frequent on T1 and T11 in the overall SAC sample. In females, T11 was the most affected vertebra; in males, there was only one individual who presented with SBO on T1 (Table 4.24). The first sacral vertebra was the most commonly affected vertebra in the overall SAC samples and the males, followed by T1 and T11 with equal numbers of presentations. For SAC females, SBO was most common on T11 (Table 4.24).

Table 4.24 Spina bifida occulta type and the specific vertebrae affected in the South African Coloured sample.

Coloured males		**Coloured females**	
SBO type	Vertebra affected	SBO type	Vertebra affected
1	T1	1	T1
1	L5	1	T11
1	S1- S2 (n=4)	1	T11-T12
2	S1-S5		

Spondylolysis

South African Coloured (SAC) males presented with both spondylolysis types (Table 4.25), while females presented with Type 2 only. However, there were more males than females who presented with spondylolysis. A bilateral occurrence was more prevalent than a unilateral occurrence in males (Table 4.25).

Table 4.25 Prevalence of spondylolysis types in South African Coloured males.

Spondylolysis type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
1 (*n*=2)	100% (*n*=2)	0	0
2 (*n*=9)	0	0	100% (*n*=9)
TOTAL (*n*=11)	18.2% (*n*=2)	0	81.8% (*n*=9)

All percentages are rounded to the nearest decimal place.

The most commonly affected vertebra in the SAC sample was L5, with the females presenting only with L5. A 45-year-old male presented with multiple-level, bilateral spondylolysis at vertebral level L4 and L5 (Table 4. 26).

In the SAC sample, the most common affected vertebra was L5 in both the male and female sample. The two female cases were bilateral on L5 (Table 4.26). In males, vertebra L2 to L5 were affected by spondylolysis. A 73-year-old male had multiple-level, bilateral spondylolysis between L3 and L5 (Table 4.26).

Table 4.26 Occurrence, vertebra affected, and age of individuals affected by spondylolysis in the South African Coloured sample.

South African Coloured males		**South African Coloured females**	
Occurrence or (unilateral bilateral)	Vertebral level affected	Occurrence (unilateral or bilateral)	Vertebral level affected
1	L3	2	L5 (*n*=2)
1	L5		
2	L4		
2	L5 (*n*=7)		
2	L4 & L5		

*1= Unilateral occurrence (Type 1) *2= Bilateral occurrence (Type 2)

South African White sample

Sacralisation

Type I (71.4%) was more prevalent than Type III (28.6%) in the SAW sample. For Type I, a unilateral occurrence was more common and left and right occurrences were equally represented (Table 4.27). A unilateral sacralisation occurrence was more prevalent.

Table 4.27 Prevalence of sacralisation types in the total South African White sample.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 71.4% (*n*=5)	40% (*n*=2)	40% (*n*=2)	20% (*n*=1)
III- 28.6% (*n*=2)	0	0	100% (*n*=2)
TOTAL (*n*=7)	28.6% (*n*=2)	28.6% (*n*=2)	42.9% (*n*=3)

All percentages are rounded to the nearest decimal place.

Both SAW males (Table 4.36) and females (Table 4.28) presented with sacralisation Types I and III. Males indicated a higher prevalence for sacralisation Type I (80%) with unilateral right (40%, *n*=2) occurrence being more prevalent than the unilateral left occurrence (20%, *n*=1) (Table 4.28). Females presented with equal numbers of Type I and III sacralisation (Table 4.29).

Table 4.28 Prevalence of sacralisation types in South African White males.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I (*n*=4)	25% (*n*=1)	50% (*n*=2)	25% (*n*=1)
III (*n*=1)	0	0	100% (*n*=1)
TOTAL (*n*=5)	20% (*n*=1)	40% (*n*=2)	40% (*n*=2)

All percentages are rounded to the nearest decimal place.

Table 4.29 Prevalence of sacralisation types in South African White females.

Sacralisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I (*n*=1)	100% (*n*=1)	0	0
III (*n*=1)	0	0	100% (*n*=1)
TOTAL (*n*=2)	50% (*n*=1)	0	50% (*n*=1)

All percentages are rounded to the nearest decimal place.

Lumbarisation

Type I was more prevalent, and a unilateral occurrence was more common, specifically on the right side. This was true for Type I lumbarisation as well (Table 4.30).

Table 4.30 Prevalence of lumbarisation types in the total White sample.

Lumbarisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I- 87.5% (*n*=7)	28.6% (*n*=2)	57.1% (*n*=4)	14.3% (*n*=1)
II- 12.5% (*n*=1)	0	0	100% (*n*=1)
TOTAL (*n*=8)	25% (*n*=2)	50% (*n*=4)	25% (*n*=2)

South African White males presented with lumbarisation Types I and II (83.3% Type I), whereas females only indicated with lumbarisation Type I (*n*=2). Furthermore, 50% of the lumbarisation cases occurred unilaterally on the right, making it the most common form in males (Tables 4.31). For females, the unilateral right was equal to the bilateral occurrence with each at 50% (*n*=1).

Table 4.31 Prevalence of lumbarisation types in South African White males.

Lumbarisation type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
I (*n*=5)	40% (*n*=2)	60% (*n*=3)	0
II (*n*=1)	0	0	100% (*n*=1)
TOTAL (*n*=6)	33.3% (*n*=2)	50% (*n*=3)	16.7% (*n*=1)

All percentages are rounded to the nearest decimal place.

Spina bifida occulta

South African White males presented with Type 1 at 88.9% (*n*=8) and Type 2 with 11.1% (*n*=1) prevalences, whereas females only presented with Type 1. Although 100% of the females presented SBO Type 1, more males presented with spina bifida occulta Type 1.

In the SAW sample, SBO was localised in the lumbo-sacral region between L4 and S5 in males while in the females, vertebrae affected were L5-S2. Spina bifida occulta occurred more frequently on S1 overall (Table 4.32).

Table 4.32 Spina bifida occulta type and the specific vertebrae affected by SBO in the South African White sample.

South African White males		**South African White females**	
SBO type	Vertebra affected	SBO type	Vertebra affected
1	L4- L5	1	L5
1	S1 (*n*=3)	1	L5
1	S1-S2 (*n*=5)	1	S1
2	S1-S5	1	S1-S2
		1	S1-S2

Spondylolysis

Type 2 spondylolysis (bilateral occurrence) was more common in the SAW sample at 68.8% (Table 4.33). Type 2 was, however, not statistically significantly higher than Type 1 (χ^2=3.125 (Yates correction), *p*=0.771).

Table 4.33 Prevalence of spondylolysis types in the total South African White sample.

Spondylolysis type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
1- 31.3% (*n*=5)	80% (*n*=4)	20% (*n*=1)	0
2- 68.8% (*n*=11)	0	0	100% (*n*=11)
TOTAL (*n*=16)	25% (*n*=4)	6.3% (*n*=1)	68.8% (*n*=11)

South African White males presented with both spondylolysis types (Table 4.34), while females only presented with Type 2. A higher prevalence for Type 2 in males was not statistically significant (χ^2 =0 (Yates correction), *p*=1). There was one male individual presenting with

multiple level Type 2 spondylolysis where L3, L4 and L5 were affected. There were more males (54.5%, *n*=6) than females (100%, *n*=5) presenting with spondylolysis Type 2.

Table 4.34 Prevalence of spondylolysis types in South African White males.

Spondylolysis type	**Sidedness (occurrence)**		
	Unilateral left	Unilateral right	Bilateral
1 (*n*=5)	80% (*n*=4)	20% (*n*=1)	0
2 (*n*=6)	0	0	100% (*n*=6)
TOTAL (*n*=11)	36.4% (*n*=4)	9.1% (*n*=1)	54.5% (*n*=6)

All percentages are rounded to the nearest decimal place.

In the SAW sample, the most commonly affected vertebra was L5 (61.1%, *n*=11). This was true for the male (69.2%, *n*=9) and female samples. (Table 4.35). The females only presented with spondylolysis on L5 (Table 4.35). In males, vertebra L2 to L5 were affected. A 73-yearold male indicated multiple-level, bilateral spondylolysis between L3 and L5 (Table 4.35). In males, L5 was the most vertebral affected segment under Type 1 (60%, *n*=3) and Type 2 (75%, *n*=6).

Table 4.35 Occurrence, vertebra affected and age of individuals with spondylolysis in the South African White sample.

South African White males		**South African White females**	
Occurrence (unilateral or bilateral)	Vertebral level affected	Occurrence (unilateral or bilateral)	Vertebral level affected
1	L2 (*n*=2)	2	L5 (*n*=5)
1	L5 (*n*=3)		
2	L5 (*n*=5)		
2	L3-L5		

*2= Bilateral occurrence (Type 2)

*1= Unilateral occurrence (Type 1)

4.5 Occurrence of multiple developmental anomalies and associated spinal pathologies

South African Black (SAB) sample

Of the 76 SAB individuals affected with some form of developmental anomaly under study, five (6.6%) individuals also presented with either multiple or single vertebral anomalies accompanied by a form of spinal pathology. The majority were males at 80% (*n*=4).

There were three SAB males (75%, *n*=3) who presented with multiple anomalies, two of these cases (66.7%) also presented with some form of spinal pathology. Furthermore, there was only one case of a female (25%) presenting with multiple vertebral anomalies only.

South African Coloured (SAC) sample

Of the 64 SAC individuals presenting with a developmental anomaly, only two individuals (a male and female) (3.1%) presented with multiple anomalies. The male presented with multiple anomalies accompanied by a spinal pathology while the female only presented with multiple vertebral anomalies.

South African White (SAW) sample

Of the 58 individuals affected with some of the developmental anomalies under study, six displayed multiple anomalies or spinal pathology. Four (66.7%) of these were males and two (33.3%) were females.

There was one (33.3%) male and two females (66.7%) presenting with multiple developmental anomalies. One of the two females also presented with some spinal pathology.

All these cases were unique in terms of the representations of developmental anomalies with spinal pathologies, therefore, no correlation could be made for any of the samples.

Chapter 5

DISCUSSION AND CONCLUSIONS

This study aimed to investigate the prevalence and pattern of developmental anomalies and their association with pathologies in the thoraco-lumbo-sacral region of South African Black (SAB), South African White (SAW) and South African Coloured (SAC). Population and sex differences have been observed in many populations (Merbs, 1974; Eubanks and Cheruvu, 2009; Walters, 2016; Garg, 2017; Parashuram *et al*., 2017; Groza *et al*., 2018; Kim *et al*., 2018; Patra *et al*., 2018) and African populations are not extensively documented. In this study, the variation among the genetically diverse groups of South Africans was assessed for comparison with the patterns discussed in the developmental anomaly literature.

5.1 Brief overview of the results

In the total sample, males presented with more developmental anomalies than females and this difference was statistically significant (χ^2= 44, p=0.00001). This indicates that males of the current South African sample are more susceptible to vertebral developmental anomalies of the thoraco-lumbo-sacral region. According to Arena *et al*. (1978), some sex-linked genes may play a role in the normal developmental during embryogenesis, for this reason their expression, overexpression or absence may cause males in this case to be more susceptible to developing certain types and/or subtypes of developmental anomalies in the thoraco-lumbosacral region. Lary and Paulozzi (2001: 247-248) proposed that some developmental anomalies may be indirectly influenced by hormonal and other physiologic differences in male and female embryos after gonadal differentiation.

Sacralisation, T13 and SBO were more prevalent in the Black South African sample of this study, while lumbarisation and spondylolysis were most common in the SAW sample. Lastly, supernumerary L6 was more common in the SAC sample. Sacralisation was the only anomaly that was statistically significantly higher between SAB and SAW, and SAC and SAW. The above observations support the suggestion that different ancestry or population groups may be more susceptible to specific vertebral developmental anomalies (Allbrook, 1955; Barnes, 1994; Roberts and Manchester, 2005).

This study has reported sacralisation, affecting the lumbo-sacral border to be the most common anomaly in the South African population. Garlowska (2001) also reported similar findings with the Neolithic remains of the Lengyel culture. In contrast, SBO is described as the most common vertebral developmental anomaly, especially in ancient skeletal material (Allbrook, 1955; Barnes, 1994; Masnicova and Benus, 2003; Sarry El-Din and El Banna, 2006; Hussien *et al*., 2008; Walters, 2016; Kim *et al*., 2019). This suggests that developmental anomalies may vary in their frequency or expression in ways that are population specific.

Sacralisation was the most common anomaly among the SAB and SAC subsamples of this study, whereas lumbarisation and T13 were the least common in those groups. The shared pattern for the SAB and SAC may be because the two groups are more genetically similar to each other than they are to the SAW (de Wit *et al*., 2009). Historically, the SAB and SAC populations were exposed to harsh environmental/social-economic factors under the apartheid regime. This included the cross-generational impacts of social stresses on pregnant women linked to epigenetics changes, difficult manual labour occupations, and nutritional insecurity.

5.2 Observation of the overall sample and subsamples of the study.

In this section, the observations of the overall, total male and female; population differences and sex differences within each population will be discussed under each developmental anomaly.

5.2.1 Sacralisation

Sacralisation was more prevalent in the SAB (7.7%, *n*=25) than in the SAC (6.6%, *n*=19) or SAW (2.4%, *n*=7) samples, and the only statistically significant difference was between the SAC and SAW samples. A similar pattern was observed in Walters' (2016) study in the Western Cape, affirming that in the South African population, sacralisation affects the SAB population more than other groups. Similarly, in the American population study (*n*=2086), which comprised the Black (*n*=1110) and White (*n*=976) samples, sacralisation was more prevalent in the Black (6.8%, *n*=75) than in the White sample (5.7%, *n*=56) (Tague, 2009). These studies, in conjunction with the present analysis, suggest that Black individuals at large, irrespective of differences in geographical areas, may be more susceptible to sacralisation.

The Hox11 gene is a crucial component in the formation of the sacral vertebra. A study done on transgenic mice has indicated that sacralisation occurs due to the overexpression of the

Hoxa11 gene in the paraxial mesoderm during development (Carapuco *et al*., 2005). Due to this overexpression, the 5th lumbar vertebra fuses to the sacrum and/or acquires sacral morphological characteristics (Carapuco *et al*., 2005; Singh, 2012; Garg, 2017). Overexpression of the Hoxa11 gene may, therefore, be triggered by several factors such as alcohol consumption, poor diet, and limited nutrient intake (calcium, riboflavin, and vitamin B_6) among pregnant women. These risk factors have been associated with an increased risk of giving birth to a child with vertebral developmental anomalies such as sacralisation in South Africa (May *et al*., 2014). A high percentage (42.8%) of pregnant women in the Western Cape, South Africa were found to be consuming alcohol during pregnancy (May *et al*., 2014). During the apartheid era, Black South Africans were clustered in townships where the main form of entertainment was gathering in alcohol outlets. This greatly increased alcohol consumption as there was little other form of entertainment and few job opportunities (Watt, *et al*., 2014). Therefore, the high prevalence of sacralisation seen in the SAB and SAC samples of this study may be suggestive of a high maternal alcohol intake during pregnancy and poor nutrient intake due to the low socioeconomic status in the SAB and SAC samples of this study.

Sacralisation was more common in males in of the overall sample and in each of the three samples of this study. Most studies reported higher prevalences in males than in females (Olofin *et al*., 2001; Sharma *et al*., 2011; Dharati *et al*., 2012; Ucar *et al*., 2013; Walters, 2016; Garg, 2017; Parashuram *et al*., 2017; Patra *et al*., 2018). This suggests that males are generally more prone to cranial border shifting at the lumbosacral border compared to females. Moreover, the male axial skeleton is more robust and heavier compared to that of the female (Mahato, 2011). Therefore, in order to transmit the heavier weight of the axial skeleton in males, the L5 vertebra in males tends to fuse to the sacrum resulting in sacralisation. This helps with the weight transmission of the axial skeleton towards the sacroiliac joint (Mahato, 2011).

In White Americans, sacralisation was more prevalent in males (3.7%, *n*=36) than in females (2%, *n*=20), also corroborating this study's results (Tague, 2009). For the Black American sample, however, sacralisation was more common in females (4.1%, *n*=45) than in males (2.7%, *n*=30) (Tague, 2009). This suggests that intra- and inter-population variation exists regarding the manifestation of sacralisation as sacralisation appears to be multifactorial in nature. For this reason, individuals with a common ancestor residing in different geographical location may not express the same pattern of a similar anomaly as they are exposed to different extrinsic factors.

Type I sacralisation, which is characterised by an enlarged transverse process without any bony union with the adjacent sacral ala, was the most common type in the overall sample.

Statistically significant differences were observed between Types I and II (χ^2 =38.4099, p<0.00001) and Types I and III (χ^2 =35.7895, p<0.00001). In Walters' (2016) study in the Western Cape, Type III was the most common form of sacralisation and this was described as a complete fusion, unilateral or bilateral, between the transitional vertebra and sacrum. Unfortunately, the unilateral and bilateral occurrences were not separated in Walters' (2016) study, limiting further comparison with the present work.

In general, a bilateral occurrence for sacralisation was more common than a unilateral occurrence among the subsamples of this study. Moreover, a unilateral left was more common than a unilateral right occurrence in the overall and in the SAB and SAC subsamples of this study. However, in the SAW sample of the current study, there was an equal unilateral occurrence on the left or right. According to Barnes (1994, 2012b), sacralisation occurs more on the right. On the contrary, in the South African sample, it appears that a bilateral occurrence is more common. What determines sidedness of sacralisation is however still unknown.

5.2.2 Lumbarisation

The rarity of lumbarisation (Barnes, 1994) was confirmed in this study where the condition was the least common among the anomalies for the overall sample as well as the SAW sample. Similar to sacralisation, lumbarisation occurs during embryonic development and is also affected by gene expression.

According to Barnes (1994), lumbarisation is generally more frequent in females than in males (Barnes, 1994). However, in the current sample, it was more common in males for the total sample and within each subsample, in fact SAB females did not present with lumbarisation. On the contrary, Walters (2016) that reported a higher prevalence of lumbarisation in females in the overall sample, with statistically significant difference. These contradictory results may be due to the different sample sizes and overall population distribution of the three ancestry groups in the two studies.

Lumbarisation was more common in the SAW sample (2.7%, *n*=8) compared to the SAC (2.1%, *n*=6) or SAB samples (0.9%, *n*=3) and these differences were not statistically significant. In Walters (2016), a higher prevalence of lumbarisation was noted in the SAC (7.9%) compared to the SAB (6.7%) or SAW (5%) samples. These results are completely different from the present study in that the SAW sample had the higher prevalence, whereas the SAW sample in Walters (2016) (*n*=300) presented with the lowest prevalence. Again, this may only reflect

different sample sizes and overall population distribution of the three ancestry groups in the two studies.

Merbs (1974:16) observed that individuals residing in the northern hemisphere tend to have a strong tendency for caudal shifting, including lumbarisation at the lumbosacral border. Although the reason is unknown, this could possibly explain the low lumbarisation prevalence observed in South African populations. Individuals residing in the northern and southern hemispheres are exposed to different climatic conditions. That is, those in the northern hemisphere are exposed to cooler temperatures than to those residing in the southern hemisphere (Kang *et al*., 2015), their diets and lifestyles are also different, suggestive of an epigenetic process as one of the possible contributing factors affecting the development of lumbarisation. This further indicates the multifactorial aetiology of lumbarisation.

Type I lumbarisation was the most common in the overall and in the total male sample of this study, but this was not statistically significant. A unilateral occurrence was more prevalent than a bilateral occurrence for the overall sample. For the total male sample, a unilateral occurrence was also more common and within the unilateral occurrence, the left side was slightly more prevalent. The total female sample had a different representation, where Type I and Type II had equal representation. For this sample, a bilateral occurrence was more common.

Furthermore, within the subsamples of the study, Type I was more common, except in SAB males where Type 2 was the most prevalent and in SAC females where there was only a Type II representation. There was a lot of variation with regards to the manifestation of the lumbarisation Types in the current South African sample. But type 1 seems to be the most common. What determines the manifestation of the expression of the different types and the sidedness of lumbarisation, remains unknown.

5.2.3 Numerical variation

It is suggested that the number of vertebrae is heritable, therefore, the variation observed between different populations would have a genetic aetiology (Tague, 2018). Supernumerary vertebrae are formed during embryological development and the main cause is somitogenesis and homeotic transformation (Tague, 2018).

5.2.3.1 13th thoracic vertebra

In the current overall sample, the prevalence of the supernumerary T13 was highest in the SAB (2.8%, *n*=9) more than the SAW (2.4%, *n*=7) and SAC (1.4%, *n*=4) samples. Also, males were more affected than females in the overall sample. Similar findings were reported for Bornstein and Peterson's (1966) North American Black and White samples.

De Beer Kaufman (1974) reported a 2.6% (*n*=12) prevalence for T13 in Black South Africans. This prevalence was also higher in males (3.6%, *n*=11) as opposed to females (0.6, *n*=1). The highest prevalence for T13 was in the small San sample (3.6%, *n*=1/28) compared to the SAB sample (2.6%) although more cases were found in the larger SAB sample.

5.2.3.2 6th lumbar vertebra

The prevalence of L6 was higher in males than in females, in agreement with several other studies on North Americans, South Africans (Black and San samples) and Americans, (Bornstein and Peterson, 1966; De Beer Kaufman, 1974; Tague, 2018). The reason for the higher prevalence in males in this study may possibly be related to the heavy male axial skeleton, where the vertebral columns of male may benefit from an extra vertebral segment to help with body weight transmission to the sacroiliac joint as with sacralisation.

5.2.4 Spina bifida occulta

A higher prevalence of SBO was observed in the SAB sample (5.2%, *n*=17), followed by the SAW (4.8%, *n*=14) and SAC (3.5%, *n*=10) samples of this study. In contrast, the White sample (*n*=245) presented with a higher prevalence than the Black sample (*n*=110) of the American population (Eubanks and Cheruvu, 2009). Walters' (2016) SBO findings did not corroborate those of this study in any way. In the Western Cape population, the SAW (28.6%) presented with a higher prevalence for SBO as opposed to the SAC (13.4%) and SAB (4.3%) samples (Walters, 2016). The difference observed among the three samples of Walters' (2016) study was statistically significant. The main difference for the conflicting results is that Walters (2016) assessed SBO in all vertebral regions, whereas the current study only focused on the thoraco-lumbosacral regions.

Eubanks and Cheruvu (2009) found that Americans with a greater sacral table angle (STA) were more prone to present with SBO. The STA represents the angle between a line drawn along the sacral end plate and a line drawn along the posterior aspect of the S1 vertebral body (Eubanks and Cheruvu, 2009:1541). This needs to be further studied in the South African

population, to explore if the association is present. Moreover, according to Husien *et al*. (2008:623), the prevalence of SBO varies by population. Although the difference was not statistically significant, this was seen in the current study where a higher prevalence was seen in the SAB than in the SAW and SAC samples. In contrast, the White samples of the American and Western Cape populations presented with higher prevalences (Eubanks and Cheruvu, 2009; Walters, 2016). These differences are inconsistent across different populations and may suggest that differences seen in relation to the expression of SBO may be population-specific (Molto *et al*., 2019). Even so, the variation with regards to SBO prevalences seen between different studies may be due to the inconsistency of recording the condition (Fidas, *et al*., 1987). For example, some studies recorded SBO in cases where the sacrum was open at the levels between S3-S5 (e.g., Albrecht, 2007; Singh, 2013; Groza *et al*., 2016), which is usually considered as a sacral hiatus (Kumar and Tubbs, 2011). Also, different researchers may also assess for the defect in different vertebral regions making it difficult to compare the results.

It has been said that the prevalence of neural tube defects such as spina bifida varies by geographical area and sociodemographic conditions, which makes it difficult to compare the expression of this defect between genetically similar populations residing in different geographical areas (Castilla and Orioli, 1985; Seller, 1987; Henneberg and Henneberg, 1999). In North Carolina, United States, SBO was uncommon in areas where women were better educated, had good access to health care, and were made aware of the importance of folic acid intake during pregnancy (Mathews *et al*., 2002).

It is suggested that the lack of access to health care facilities is one of the leading causes of SBO in South Africa (Mashiloane and Masekela, 2020). This may explain the high prevalence seen in the SAB sample under study, especially as those individuals lived during the apartheid era where they were discriminated against and oppressed. The fact that Black South Africans were forcefully moved to the homelands during the 1960s made it difficult for them to access proper health care and facilities with the proper resources necessary for their health needs as these facilities were mostly in the urban areas which were occupied by the White South Africans (Baker, 2020). The high prevalence of SBO in the Black South African sample may reflect poor access to prenatal care and folic acid supplements combined with dietary insufficiency. However, if lack of access to health care facilities was the only cause of SBO, then we would have observed the lowest prevalence in the SAW and not in the SAC sample. Conditions such as maternal obesity, diabetes, and intake of anticonvulsants during pregnancy are also

associated with a higher risk of giving birth to a child with neural tube defects (Josan *et al*., 2008). This may explain the observed prevalence for SAW in this study.

5.2.5 Spondylolysis

This condition was more common in the SAW than the SAC or SAB samples. White individuals in general have low bone mineral densities, therefore, less bone strength which predisposes them more to osteoporosis and subsequent bone fractures in the spine (Hochberg, 2007), as observed with spondylolysis.

Previous studies based on the South African population reported higher prevalences of spondylolysis in males than in females; this corroborates the findings of this study specifically for the SAC and SAB samples (Eisenstein, 1978; Van der Merwe *et al*., 2010; Walters, 2016). Eisenstein (1978) reported a higher prevalence in White females (5.7%) than in males (3.8%) of the South African population. This contradicts the findings of this and Walters' (2016) study. However, the comparison with Eisenstein (1978) may not be reliable as the actual number of individuals affected by spondylolysis was not provided.

Most non-South African studies report a higher prevalence in males (Gunness-Hey, 1981; Bradtmiller, 1974; Fibiger and Knüsel., 2005; Weiss, 2009; Pilloud and Canzonieri, 2014; Sakai *et al*., 2016; Kim *et al*., 2018). The higher prevalence of spondylolysis in Black and Coloured South African males may be due to the gender-based activities undertaken where males tend to undertake more strenuous activities (Walters, 2016).

In the total sample of this study, spondylolysis occurred more often bilaterally (2.5%, n=23) than unilaterally (0.8%, n=7), which supports the results of most studies (Gunness-Hey, 1981 Koniag sample, Eskimos; Frederickson *et al*., 1984; Mays, 2006- Medieval English). Eisenstein (1978) and Walters (2016) also observed more bilateral than unilateral occurrences in the South African population. In fact, Walters (2016) did not observe any unilateral occurrences in the 8 incidences of the Western Cape sample. This affirms that bilateral occurrence is more common in the South African population.

Spondylolysis is usually asymptomatic; therefore, most individuals live their lives not knowing they possess the defect (Roberts and Manchester, 2005; Syrmou *et al*., 2010; Mora de sambricio and Garrido-Stratenwerth, 2014; Nakayama and Ehara, 2015; Sakai *et al*., 2016; Gagnet *et al*., 2018). For this reason, the unilateral defect easily progresses resulting in a bilateral separation (spondylolisthesis) (Shore, 1930; Merbs, 1989, 2002; Arriaza, 1997; Ortner, 2003; Roberts and

Manchester, 2005; Syrmou *et al*., 2010; Leone *et al*., 2011; Morade Sambricio and Garrido-Stratenwerth, 2014).

Aside from athletic activities, factors affecting the prevalence of spondylolysis in the South African population may include interfacet distance and pelvic incidence (Ward and Latimer, 2005; Vialle *et al*., 2007; Oh *et al*., 2009; Chung *et al*., 2012; Ward *et al.,* 2010; Chung *et al*., 2012). Individuals with increased interfacet distances inferiorly (from L1-S1) are less likely to develop spondylolysis (Ward and Latimer, 2005; Ward *et al.,* 2010; Chung *et al*., 2012). Moreover, lumbar lordosis, pelvic tilt, pelvic incidence and pelvic slope (as seen in radiological reviews) have been found to be s in individuals presenting with spondylolisthesis (Vialle *et al*., 2007; Oh *et al*., 2009; Chung *et al*., 2012). Future studies investigating factors of these parameters in the South African population are necessary to determine their association with spondylolysis.

The vertebra most affected by spondylolysis in the overall study sample was L5; this was also true for the three subgroups. Most studies reported similar results (Haukipuro, *et al*., 1978; Bridges, 1989; Merbs, 1989; Arriaza, 1997, 2002; Roberts and Manchester, 2005; Mays, 2006; Nakayama and Ehara, 2015). Spondylolysis occurs more frequently on L5 due to the repetitive load bearing function it has, as most of the body weight is transmitted inferiorly (Mays, 2006; Tawfik *et al*., 2020). Spondylolysis was observed from L2 to L5 in the current South African sample. In the SAC subsample, however, affected vertebra was between L3- L5.

Similar to Eisenstein's (1978) observations, spondylolysis did not seem to be affected by age as there was no clear pattern between the number of individuals affected and age. Also, the progression from a unilateral to a bilateral occurrence could not be confirmed.

Association with other anomalies and pathologies

Due to the general genetic/epigenetic aetiology of vertebral developmental anomalies, the cooccurrence of the different conditions would not be unexpected. Factors that play a role in the expression of developmental anomalies have impacts on specific stages of the developmental process. These factors may affect different regions of the body, therefore, producing multiple anomalies (Roberts and Manchester, 2005). Eubanks and Cheruvu (2009) found a positive association between spondylolysis and SBO in their assessment of Black and White Americans. Additionally, the consequent changes to the weight-bearing and

biomechanical dynamics of the spine and pelvis would be expected to change the risks for vertebral pathologies that develop during life.

Sacralisation of L5 has been said to cause disc herniation and early degeneration of the vertebra above the sacralised vertebra (Elster, 1989; Barnes, 1994; Vergauwen *et al*., 1997; Luoma *et al*., 2004; Bron *et al*., 2007; Ravikumar *et al*., 2013; Sekharappa *et al*., 2014; Singh, 2014; Nayak, 2016). Two individuals aged 66 and 87 years, who presented with sacralisation and Schmorl's nodes on T12 and upward indicating that there was disc degeneration and herniation. According to Nerlich *et al*. (1997), the onset of intervertebral disc degeneration begins around the age of 20 years. For this reason, it is difficult to confirm if the pathology observed on dry bone is due to the presence of a developmental anomaly or if it is due to normal age-related changes.

Vertebral body compression was observed in three of the of the four bilateral spondylolysis cases. While the specific vertebra compressed was not the same in all cases, it was consistently above the vertebra affected by spondylolysis but not in all cases directly adjacent to the spondylolysis occurrence. Vertebral compression fractures are common in older individuals, especially in White and Asian Americans more than in African Americans (Alexandru and William, 2012). The individuals who presented with bilateral spondylolysis were 55 years and older. Thus, the vertebral compression observed may have been related to ageing.

Some individuals presented with multiple developmental anomalies, for example, block vertebra, which was not part of the developmental anomalies of interest, was observed in three of the four sacralisation cases. The types of sacralisation were unique in all the three cases; therefore, no association could be made between the presence of a block vertebra and the type of sacralisation. Two of the sacralisation cases had a bilateral representation, while one was a unilateral case.

Furthermore, in addition to block vertebra and sacralisation, one case also presented with Type 1 spina bifida occulta. It is possible for an individual to express multiple unrelated anomalies (Roberts and Manchester, 2005). Therefore, no clear pattern was observed in relation to the presentation of some multiple anomalies. Du Plessis (2017) did not find a direct association between thoracolumbar transitional vertebrae and other vertebral anomalies such as spondylolysis, neural tube defects and sacro-coccygeal fusion in 35 identified cases.

It is difficult to confirm the effect of developmental anomalies on the biomechanics of the vertebral column with a sample that is mostly comprised of older individuals. Therefore, a

sample with younger individuals would be required to provide more accurate observations and results with regards to the association between developmental vertebral anomalies and spinal pathologies. This is the main reason why osteoarthritic changes such as osteophytic lipping were not considered in this study.

CONCLUSION

This is the first study to compare six developmental anomalies (sacralisation, lumbarisation, T13, L6, SBO and spondylolysis) in large samples of Black, Coloured and White components of the South African population. From this study, it can be said that males are more susceptible to vertebral developmental anomalies and the most common developmental anomaly in the South African population is sacralisation, with the least common being lumbarisation.

The aetiology of most of these anomalies seems to be multifactorial in nature, however, low socio-economic status, insufficient nutrient intake during pregnancy and the lack of access to health care facilities that are consequences of poverty seems to be the major factors that contribute to giving birth to a child with vertebral developmental anomalies in South Africa. This is, among other reason, why most anomalies are more common in South African Blacks, more than in other South African groups.

Associations between the developmental anomalies and other spinal pathologies indicated that vertebral developmental anomalies of the thoraco-lumbo-sacral region may compromise the biomechanics of the vertebral column predisposing it to spinal pathologies, however, it is not always possible to associate the vertebral anomalies to spinal pathologies in older individuals as normal degenerative changes are also interfering with the biomechanics of the spinal column. Furthermore, most skeletal remains are of older individuals and normal degenerative changes are already expected to be seen.

In addition, although the differences observed for the different developmental anomalies in this study were not statistically significant, there were substantial sex and ancestry differences in and among the three samples of the study. Inter- and intra-population differences, as well as biological sex, should, therefore, be considered when dealing with these developmental anomalies in biological anthropological or clinical contexts.

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Appendix 1

Table A.1. Prevalence of sacralisation across populations

Author	**Sample size (*n*)**	**Population**	**Type of study**	**Prevalence**
Allbrook, 1955	206	East African	Dry bone	11% (*n*=22)
Merbs, 1974	70	Sadlermiut Eskimos	Dry bone	5.7%
	78	Northwest Coast Indians		4.3%
Henneberg & Henneberg, 1999	124	Pompeii sample-Italians (79 AD)	Dry bone	19% M=23% F=13%
Olofin *et al*., 2001	112	Lagos Nigerians	Radiological	64% (M=48%) (F=16%)
Masnicova & Benus, 2003	112	Devı ´n-Hrad sample	Dry bone	8% (*n*=9) M=15% (*n*=7/46) F=2% (*n*=1/53) Non-sexed=8% (*n*=1/13)
	29	Devı ´n-Za kostolom sample		7% (*n*=2) M=6% (*n*=1/16) F=8% (*n*=1/13)
Chaijaroonkhanarak *et al*., 2006	206	Thai skeletons	Dry bone	4.4% (*n*=9) M=6.1% (*n*=7) F=2.2%) (*n*=2)
Sarry El-Din & El Banna, 2006	272	Ancient Egyptians	Dry bone	1.48% (*n*=4) M=0.74% (*n*=1) F=2.2%) (*n*=3)
Tague, 2008	M=1048 F=1038	American Blacks and American Whites	Dry bone	Total prevalence: 6.3% Blacks: M(*n*=30), F(*n*=45) Whites: M(*n*=36) F(*n*=20)
Sharma *et al.*, 2011	206	Central Indians	Dry bone study	14.1% (*n*=29) M=69% (*n*=20) F=31%) (*n*=9)
Dharati *et al*., 2012	189	Gujarat Indians	Dry bone	11.1% (M=12.2%) (F=9.5%)
Deepa & Martin, 2013	117 M(*n*=70) F(*n*=47)	South Indians	Dry bone study	10.25% (*n*=12) M(*n*=8) F(*n*=4)
Khairnar & Rajale, 2013	60	Not provided	Dry bone study	6.6% (*n*=4)

Author	Sample size (*n*)	Population	Type of study	Prevalence
Toneva & Nikolova, 2013	147	Drustar (Silistra), Bulgaria (medieval necropolis)	Dry bone	2% (*n*=3)
Ucar *et al*., 2013	3607	Turkish	Radiological	17% (M=19.5%) (F=15%)
Yavuz *et al*., 2013	5000	Turkish males	Radiological	4.4% (*n*=222)
French *et al*., 2014	5941	Australian	Radiological	4.1%
Sekharappa *et al*., 2014	Not provided	Not provided	Radiological	11%
Singh, 2014	60	North Indians	Dry bone	16.6% (*n*=11)
Singh *et al.*, 2014	20 M= (*n*=10) F= (*n*=10)	Not provided	Dry bone	6.6% (*n*=3) M= (*n*=2) F= (*n*=1)
Singh & Singh, 2015	30	Not provided	Dry bone	6.7% (*n*=2)
Krishnamurthy and Adibatti, 2016	50	South Indian	Dry bone	6% (*n*=3)
Nayak, 2016	80	Eastern Indians	Dry bone	15% (*n*=12)
Tins & Balain, 2016	420	Not provided	MRI	*N*=8 M: (*n*=3) F: (*n*=5)
Walters, 2016	300	South Africans: Western Cape population	Dry bone	12% (*n*=35) M= 13.3% F=10.4%
Garg, 2017	100	Not provided	Cadaveric (dry bone)	17% (*n*=17) M= 18.03% (*n*=11/61) F=15.39% (*n*=6/39)
Parashuram *et al.*, 2017	100	Not provided	Dry bone	16% (*n*=17): M=10% (*n*=10) F=6% (*n*=6)
Akinyi, 2018	167	Uganda population	Radiological	82%*(*n*=14)
Groza *et al*., 2018	79	Iasi, Romans	Dry bone	3.79% (*n*=3)- all males
Kim *et al.*, 2018	198 M= (*n*=81) F= (*n*=68)	Asians	Dry bone	5.1% (*n*=10) M= 12.3% (*n*=10/81) F= 4.4% (*n*=3/68)
Patra *et al*., 2018	50	North Indians	Dry bone	8% (*n*=4) All males
Abutaher & Avinash, 2019	98	Indians	Dry bone	18.33% (*n*=18)

*****Highest prevalence. M- males. F-females

Table A.2 Prevalence of lumbarisation across populations.

Source	Sample size (*n*)	Population	Type of study	Prevalence %
Merbs, 1974	70	Sadlermiut Eskimos	Dry bone	34.3%
	78	Northwest Coast Indians		32.9%
Jankauskas, 2001	857	Lithuanian	Dry bone	M=8.64±1.51% F=4.42±1.30%
Olofin *et al*., 2001	112	Lagos population	Radiological	36%*
Masnicova and Benus, 2003	112	Devı ´n-Hrad sample	Dry bone	2% (*n*=2) M=2 (*n*=1/46) F=2% (*n*=1/53)
	29	Devı ´n-Za kostolom sample		0%
Sarry El-Din and El Banna, 2006	272	Ancient Egyptians	Dry bone	0.74% (*n*=2) M=0.74% (*n*=1) F=0.74% (*n*=1)
Mahato, 2010	332	India*	Dry bone	3.9% (*n*=13)
Sharma *et al.*, 2011	206	Central Indians	Dry bone	4.3% (*n*=9) M=66.7% (*n*=6) F=33.3% (*n*=3)
Dharati *et al*., 2012	189	Gujarat Indians	Dry bone	1.6% (M=0.7%) (F=2.7%)
Deepa & Martin, 2013	117 M= (*n*=70) F= (*n*=47)	South Indians	Dry bone	1.7% (*n*=2) M= (*n*=1) F= (*n*=1)
Ucar *et al*., 2013	3607		Radiological	1.7% (M=1.4%) (F=2.1%)
Yavuz *et al*., 2013	500	Turkish males	Radiological	1.2% (*n*=59)
French *et al*., 2014	5941	Australian population	Radiological	5.8%
Sekharappa *et al*., 2014		India* not stated	Radiological	2%
Singh & Singh, 2015	30	Not provided	Dry bone	6.7% (*n*=2)
Tins & Balain, 2016	420	Not provided	MRI	*n*=4 (M=3) (F=1)
Walters, 2016	300	Cape Coloureds	Dry bone	7.3% (*n*=21) M= 4.7% F= 12.6%
Akinyi, 2018		Uganda population	Radiological	18%
Groza *et al*., 2018	79	Iasi, Romans*	Dry bone	1.26% (*n*=1)
Kim *et al.*, 2018	198	Asians	Dry bone	3.0% (*n*=6) M= 1.2% (*n*=1/81) F= 1.5% (*n*=1/68)

Patra *et al*., 2018	50	North Indians	Dry bone	4% (*n*=2) All females
Abutaher & Avinash, 2019	98	Not provided	Dry bone	18.33% (*n*=18)

*****Highest prevalence. *n*- number of individuals. M- males. F-females

A.3 revalence of 13th thoracic vertebra.

Source	**Sample size**	**Population**	**Type of study**	**Prevalence %**
Allbrook, 1955	206	East Africans	Dry bone	4.4% (*n*=9)
De Beer Kaufman, 1974	462	Black South Africans	Dry bone	2.6% (*n*=12) M=3.6% (*n*=11) F=0.6% (*n*=1)
	28	San population (Bushman)		3.6% (*n*=1) M=3.6% (*n*=1) F=0
Merbs, 1974	70	Sadlermiut Eskimos	Dry bone	15.7%* (*n*=11)
	78	Northwest Coast Indians		12.8% (*n*=10)
Tague, 2018	M=1318 F=407	African American and Europeans Americans	Dry bone	M=3% (*n*=40) F=6.9% (*n*=28)

*****Highest prevalence. *n*- number of individuals. M- males. F-females

A.4 revalence of the sixth vertebra across populations.

Author	**Sample size**	**Population**	**Type of study**	**Prevalence %**
Allbrook, 1955	200	East Africans	Dry bone	7.5% (*n*=15)
Bornstein & Peterson, 1966	Overall sample: 1239	North Americans	Dry bone	Overall sample: 2.3% (*n*=28) M= 0.7% (*n*=9) F= 1.5% (*n*=19)
	234	Mongoloid		6.4% (*n*=15) M= 1.7% (*n*=4) F= 4.7% (*n*=11)
	488	Caucasoid		1.6% (*n*=8) M= 0.6% (*n*=3) F= 1.0% (*n*=5)
	517	Negroid		1.0% (*n*=5) M= 0.4% (*n*=2) F= 0.6% (*n*=3)
De Beer Kaufman, 1974	462	Black South Africans	Dry bone	8.2% (*n*=38) M= 10.5% (*n*=32) F= 3.8% (*n*=6)
	28	San (Bushman)		14.3%* (*n*=4) M= 10.7% (*n*=3) F= 3.6% (*n*=1)
Merbs, 1974	70	Sadlermiut Eskimos	Dry bone	4.3% (*n*=3)
	78	Northwest Coast Indians		14.1% (*n*=8)
Apazidis *et al.*, 2011	211		Radiological	6.6% (*n*=14)
Kim *et al.*, 2018	M=81 F=68	Asians	Dry bone	1.3% (*n*=2/149) M=1.2% (*n*=1/81) F=1.5% (*n*=1/68)
Tague, 2018	M=1318 F=407	African American and European Americans	Dry bone	M=6.4% (*n*=85) F=2.7% (*n*=11)

*****Highest prevalence. *n*- number of individuals. M- males. F-females

A.5 Prevalence of spina bifida occulta

Source	**Sample size**	**Population**	**Type of study**	**Prevalence**
Shore, 1930	82	Black South Africans	Dry bone	28% (*n*=23)
Allbrook, 1955	200	East Africans	Dry bone	10%
Fidas *et al*., 1987	235	Cumbernauld population sample	Radiological	23% M=30% F=17%
Bradtmiller, 1974	100 (M=58) (F=42)	Arikara, Sully sample	Dry bone	2% M=3.4% F=0
	75 (M=43) (F=32)	Arikara, Larson sample		9.3% M=11.6% F=6.3%
Rosenberg *et al*., 1981	143	Ohio	Radiological	8.4% (*n*=12)
Saluja, 1988	112	Historic London	Dry bone	15.2%
	140	Modern London		15.7%*
Henneberg & Henneberg, 1999	124	Pompeii sample	Dry bone	11% M=36% F=61%
Masnicova & Benus, 2003	109	Devı ´n-Hrad sample	Dry bone	24% (*n*=26) M=26% (*n*=11/43) F=19% (=10/52) Non sexed= 36% (*n* =5/14)
	26	Devı ´n-Za kostolom sample		23% (*n*=6) M=36% (*n*=5/14) F=9% (=1/11) Non sexed= 0% (*n*=0/1)

Sarry El-Din & El Banna, 2006	272	Ancient Egyptians	Dry bone	3.33% (*n*=9) M=5.18% (*n*=7) F=1.48%) (*n*=2)

Source	Sample size	Population	Type of study	Prevalence
Eubanks & Cheruvu, 2009	2866	African Americans and Whites	Dry bone	12.4% (M=13.2%; F=8.3%) (Whites=14.2%) (Blacks=9.8%)
Simalcsik *et al.*, 2011	129	European, Medieval population from Iași	Dry bone	1.55% (*n*=2)
Toneva & Nikolova, 2013	147	Drustar (Silistra), Bulgaria (medieval necropolis)	Dry bone	2% (*n*=3)
Yavuz *et al*., 2013	500	Turkish males	Radiological	10.2% (*n*=510)
Ali *et al*., 2014	200	Pakistanians	Dry bone	34.5%* (*n*=69)
Walters, 2016	300	Cape Coloured, Blacks and White South Africans	Dry bone	14% (*n*=42) M= 12.9% F= 16.5%
Groza *et al*., 2018	79	Iasi Romans*	Dry bone	3.79% (*n*=3) (all males)
Kim *et al.*, 2018	M=81 F=68	Asians	Dry bone	7.6% (*n*=15) M= 12.3% (*n*=10/81) F= 4.4% (*n*=3/68)
Molto *et al*., 2019	442	Egyptians (Ain Tirghi, Kellis 2 (K2) and the Kellis village site)	Dry bone	Overall sample:15.6% (*n*=69/442) M= 21.1% (*n*=40) F= 11.5% (*n*=29) <u>Kellis sample: 17.7%</u> M=24.3% (*n*=25) F=13% (*n*=19) <u>Ain Tirghi sample: 13%</u> M=17.2% (*n*=15) F=9.4% (*n*=10)

*****Highest prevalence. *n*- number of individuals. M- males. F-females

Table A.6 The prevalence of spondylolysis from previous studies.

Source	**Sample size**	**Population**	**Type of study**	**Prevalence**
Allbrook, 1955	200	East Africans	Dry bone	5%
Lester & Shapiro, 1968	Total N 295	Pre-historic American Eskimos	Dry bone	41% (n=121)
	248	Tigara		45% (*n*=111)
	47	Ipiutak		21% (*n*=10)
Bradtmiller, 1974	100 (M=58) (F=42)	Arikara, Sully sample	Dry bone	11.7% M=12.3% F=10.6%
	75 (M=43) (F=32)	Arikara, Larson sample		25.8% M=28.2% F=23.3%
Eisenstein, 1978	485	Black and White South Africans	Dry bone	3.5% Black sample: M=3.5% F=2.6% White sample: M=3.8% F=5.7%
Gunness-Hey, 1981	175	Koniag Eskimo	Dry bone	25.7% (*n*=45) M=36.1% (n=26) F=25.8% (*n*=17)
Rosenberg *et al*., 1981	143	*Ohio*	Radiological	0%
Bridges, 1989	M=23 F=20	Archaic Indians	Dry bone	M=17% (*n*=4/23) F=20% (*n*=4/20)
Waldron, 1991	214	Romano-British	Dry bone	3.74% (M=3.79%) (F=3.66%)
	110	Anglo-Saxon		4.55% (M=3.64%) (F=5.45%)
	629	Medieval		5.08% (M=5.01%) (F=5.20%)
	706	18th/19th centuries		1.42% (M=2.22%) (F=0.58%)
Merbs, 1996	180	Alaskan	Dry bone	4.4% (*n*=8)
	193	Canadian Inuits		4.1% (*n*=8)

Source	Sample size	Population	Type of study	Prevalence
Arriaza, 1997	38	Hyatt population, Guam	Dry bone	21% (*n*=8) M=29.4% (5/17) F=14.3% (3/21)
Jankauskas, 2001	857	Lithuanian	Dry bone	6.5%
Merbs, 2002	417	Inuits (Artic Canada)	Dry bone	*n*=90 M= 0.70% (*n*=62) F= 0.30 (*n*=26) Additional 2 individuals (unknown sex)
Masnicova & Benus, 2003	136	Devı ´n-Hrad sample	Dry bone	7% (*n*=10) M=8% (*n*=4/53) F=8% (=5/65) Non sexed= 6% (*n* =1/18)
	45	Devı ´n-Za kostolom sample		4% (*n*=2) M=8% (*n*=2/24) F=0% (=0/17) Non sexed= 0% (*n*=0/4)
Fibiger & Knüsel, 2005	310	British	Dry bone	5% (*n*=16)
Mays, 2006	210	Medieval English Skeletal Population (Wharram Percy, England)	Dry bone	11.9% (*n*=24) M=14.5% (*n*=16/110) F=8.9% (=8/90)
Mays, 2007	239	Medieval English Skeletal Population (Wharram Percy, England)	Dry bone	Non adults=0.7% Adults=12%
Masharawi *et al*., 2007	M=2374 F=700	Caucasion and African Americans	Dry bone	M= 4.6% (*n*=109) F= 0.9% (*n*=6)

Weiss, 2009	146	Pre-contact, San Francisco	Dry bone	16.4% (*n*=24) M=26% (*n*=17) F= 11% (*n*=7)
Source	**Sample size**	**Population**	**Type of study**	**Prevalence**
Lessa, 2011	81	Brazilians	Dry bone	29.6% (*n*=24) M=33.3% (*n*=16) F= 24.2% (*n*=8)
Jiménez-Brobeil *et al.*, 2012	Not provided	Medieval, (La Torrecilla) North Spain	Dry bone	M=2.9% (*n*=1/35) F=7.1% (*n*=2/28)
		Medieval, (Villanueva de Soportilla) South Spain		M=14.3% (n=3/21)
Chen *et al.*, 2013	120	Blacks and Whites (*Hamman-Todd collection)	Dry bone	3.87% (*n*=120)
Pilloud & Canzonieri, 2014	46	Pre-contact, California	Dry bone	17.4% (*n*=8) M= 30.8%(*n*=4/13) F= 12.1% (*n*=4/33)
Walters, 2016	300	Cape Coloured, Blacks and White South Africans	Dry bone	2.7% (*n*=8) M= 13.0% F= 1.0%
Kim *et al.*, 2018	198	Asians	Dry bone	3.0% (*n*=6) M= 3.7% (*n*=3/81) F= 2.9% (*n*=2/68)

*****Highest prevalence. *n*- number of individuals. M- males. F-females

Appendix 2: Scoring criteria for the developmental anomalies and vertebral pathologies

Lumbo-sacral border

Table A7 Sacralisation

Type	**Score ()**	**Description**
Absent	0	No evidence of cranial shifting
Type I: A: Unilateral B: Bilateral	**Type IA** Unilateral- (1) **Type IB** Bilateral- (2)	Incomplete sacralisation characterised by an enlarged transverse process without any bony union with the adjacent sacral ala
Type II: A: Unilateral B: Bilateral	**Type IIA** Unilateral- (3) **Type IIB** Bilateral- (4)	Complete sacralisation will be characterised by enlarged transverse process with complete fusion with the adjacent sacral ala
Type III	(5)	Mixed feature presents with unilateral Type I on one side and unilateral Type II on the other

*Scoliosis was also scored as present or absent to determine the association with sacralisation. The presence of scoliosis was determined by the lateral curvature of the vertebral column after articulation of successive vertebra

Table A8 Lumbarisation

TYPE	**Score**	**Description**
Absent	0	No evidence of caudal shifting
Type I A. Unilateral B. Bilateral	Type IA Unilateral- 1 Type IB Bilateral- 2	Incomplete lumbarisation, which is the incomplete separation of the first sacral body from the adjacent sacrum, presented by an anterior cleft on the anterior aspect of the sacral body
Type II	3	Complete lumbarisation, which is the complete separation of the first sacral segment from the adjacent sacrum, presented by the absence of a bony union

Table A9 13th thoracic vertebra

Presence	**Score**	**Description**
Absent	0	Absence of extra/13th thoracic vertebra
Present	1	Presence of 13 thoracic vertebrae instead of 12 at the thoraco-lumbar border. May present with or without articulating rib facet, depending on the characteristics of the border acquired.

Table A10 Sixth lumbar vertebra

Presence	**Score**	**Description**
Absent	0	Absence of extra/sixth lumbar vertebra
Present	1	Presence of 6 lumbar vertebrae instead of 5 at the lumbo-sacral border. May be fused or unfused to the sacrum.

Table A11 Spina bifida occulta

Presence	**Score**	**Description**
Absent	0	No evidence of spina bifida
Incomplete	1	Vertebra above the fourth sacral segment affected
Complete	2	All sacral segments affected

*The presence spondylolysis and spondylolisthesis were noted in association with spina bifida occulta

Table A12 Spondylolysis

Presence	**Score**	**Description**
Absent	0	No evidence of Spondylolysis
Complete fracture	1	Unilateral separation at the pars interarticularis
Spondylolisthesis	2	Bilateral separation at the pars interarticularis

Appendix 3: ethics letter

School of Anatomical Sciences

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SCHOOL OF ANATOMICAL SCIENCES ETHICS WAIVER CLEARANCE LETTER

Faculty of Health Sciences School of Anatomical Sciences University of the Witwatersrand Johannesburg

Re: In terms of Chapter 8, sections 62-64 of the National Health Act No 61 of 2003 donated bodies and their tissues may be used for, among other purposes, health and research. Use of such Material is subject only to permission from the responsible person in the School of Anatomical Sciences - the Head or person designed by the Head.

Human Research Ethics Committee (Medical) Clearance Certificate:

W-CJ-140604-1

This letter serves to confirm that the Head of School, based in the School of Anatomical Sciences, Faculty of Health Sciences, has reviewed the research proposal entitled ***An assessment of developmental anomalies in the thoraco-lumbo-sacral region of South Africans*** and has granted clearance to access the blanket ethics waiver to conduct the abovementioned research study.

Yours sincerely

Dated 16th April 2020



Professor Maryna Steyn
Head: School of Anatomical Sciences