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Profile of patients with Blount’s disease at an Academic Hospital

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Profile of Patients with Blount's disease at an Academic Hospital



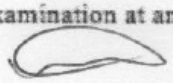
Mohammed Mehtar

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Medicine

Johannesburg, 2017

Declaration

I Mohammed Mehtar declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Medicine in the Branch of Orthopaedic Surgery at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



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(Signature of candidate)

23 day of October 2017 in Johannesburg

Presentations arising from research project

Abstract submitted to South African Orthopaedic Association, Annual Congress, Oral Presentation. September 2017. Port Elizabeth.

Publications arising from research project

None

Abstract

Introduction

Despite an increased incidence of Blount's disease in South Africa, the aetiology is unknown with a historical predisposition attributable to an early walking age, large stature, obesity, Black African race and genetics. The aim of this study is to explore the profile of patients with Blount's disease seen at an Academic Hospital.

Materials and Methods

This is a retrospective case series with an evaluation of hospital and outpatient records (data sheets) of children diagnosed with Blount's disease (Infantile, Juvenile and Adolescent Groups) from 01 January 2003 to 31 December 2016. Demographic information including age when the deformity was first noticed, age at presentation, gender, race, weight, height, milestones, bilateral involvement and family history were documented.

Results

Data was available for 108 patients with a total of 172 involved limbs. In this series all patients were of Black African race. There were 12 documented cases with a family history of bow legs (seven in the Infantile Group, five in the Juvenile Group and zero in the Adolescent Group). The developmental milestones of patients within all three groups were within normal limits and in particular were not early. The majority of the patients in the Infantile and Juvenile Groups were female whereas the Adolescent Group had a male predominance. There was a similar occurrence of bilateral involvement in both the Infantile Group (64%) and the late-onset group (56%). The median BMI for patients in the Infantile Group was lower than that for children in the Juvenile and Adolescent Groups (19.49, 28.5 and 33.4 respectively). A greater proportion of male patients were classified as obese compared to female patients (82% *versus* 50%) and there was no significant difference with the BMI of patients with unilateral and bilateral deformity.

Conclusion

In this population, this study confirms a heritable component in Blount's disease (20%). Early-onset walking age was not a risk factor for Infantile Blount's disease. There was a

female preponderance in the Infantile and Juvenile Groups but a male preponderance in the Adolescent group. The BMI increased with increasing age. A greater proportion of male patients were classified as obese compared to female patients for reasons undetermined (82% *versus* 50%). No risk factors were found for unilateral involvement. This paper has helped to elucidate the above mentioned facts in this population of patients with Blount's disease.

Acknowledgements

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Nomenclature

USA – United States of America

CHBAH – Chris Hani Baragwanath Academic hospital

BMI – Body mass index

MDA – Metaphyseal diaphyseal angle

CEO – Chief Executive Officer

CDC - Centers for Disease Control and Prevention

ANOVA - Analysis of variance

HREC - Human Research Ethics Committee

CHAPTER 1

1 Introduction and literature review

1.1 Background

Blount's disease is a developmental disorder presenting in childhood and results in multiplanar deformities of the lower limb.[1-3] The disease was first reported by Erlacher[4] in 1922 and this was followed by a detailed description by Blount[5] in 1937. Langenskiold[6] described a progression of radiographic changes associated with the disease in a Scandinavian population.

The deformities that develop secondary to relative inhibition of the posteromedial aspect of the proximal tibial growth plate include tibial varus, procurvatum, internal rotation and limb shortening.[1-3] This leads to a progressive deformity resulting in premature arthritis of the knee.[7,8]

Blount's disease can be classified into two types dependent on the age of onset with early-onset, or Infantile, occurring under the age of four and late-onset occurring after the age of four years. Late-onset Blount's disease can be further classified as a Juvenile type (onset at age four to ten years) or an Adolescent type (onset after the age of ten years).[9]

The estimated prevalence of Blount's disease is less than 1% in the United States of America (USA)[10] and in South Africa (Western Transvaal) it was estimated by Bathfield and Beighton[11] to be 0,03%. There is an increased occurrence of Blount's disease in South Africa.[11]

Predisposition for Blount's disease has been attributed to early walking age, large stature, obesity, race and genetics.[12]

With regards to ethnicity, in the USA it has been reported that there is an increased prevalence of Infantile Blount's disease in the African American and Hispanic population than in European or Asian groups.[13] A review by Bradway, Klassen and Peterson[14] found that blacks are more commonly affected than whites and the deformity is more common in the West Indies, Finland and Africa. Bathfield and Beighton[11] had no instances of Blount's disease in white or Indian children and all patients in their series were blacks (Baragwanath hospital only treated black patients during the apartheid years when this study was carried out). Why the disease predominantly affects black patients has not been elucidated.

Blount's disease is noted with an increased frequency in overweight children.[9,15-17] A large percentage of patients treated with Infantile Blount's disease are greater than the 95th percentile of weight for age as reported in a number of studies in the USA.[17-21] The Heuter-Volkmann principle of asymmetric growth inhibition resulting from increased compressive forces on the medial physis can explain the pathogenesis of genu varum in Blount's disease.[22,23] The compressive forces on the medial aspect of the proximal tibia is markedly increased in obese children with genu varum.[17,24] Cook *et al*.[25] using finite element analysis found that obesity caused forces strong enough to retard growth in the physis. Davids, Huskamp and Bagley[26] examined gait deviations associated with obesity and found that an obese child had difficulty with hip adduction and produced the supposed 'fat-thigh gait.' This gait produces a varus moment on the knees and increases compressive forces across the medial part of the proximal tibia to inhibit physeal growth. Gushue, Houck and Lerner[24] compared biomechanics of the knee joint in normal and overweight children and confirmed the higher abduction moment of the knee during the stance phase with greater medial compartment loading of the knee joint. Sabharwal, Zhao and McClemens[22] found that children with Infantile Blount's disease had a more severe proximal tibial deformity compared to the Adolescent Group despite their BMI being lower. Obese black children with Blount's disease may have a poorer prognosis than other children and adolescents.[1,16,23,27] Bathfield and Beighton[11] reported no difference with regards to early walking age or obesity in children with Blount's disease compared to unaffected children but did not provide any specifics about the BMI, weight or x-ray findings of the children. White *et al*.[28] in their review of late-onset Blount's patients in Cape Town had 61% obese patients (53% of Juvenile and 74% of Adolescent patients) in contrast to international studies which had over

90% obese patients. Why some obese children have unilateral involvement and why some children with Blount's disease are not overweight remains unknown.[1,22]

White *et al*.[28] reported a 2:3 male to female ratio of Blount's disease in the late-onset Group, which contrasts with international statistics which showed a male to female ratio of 4:1. With regards to Infantile Blount's disease, Bradway *et al*.[14] found that boys and girls were equally affected. Bathfield and Beighton[11] in their series of patients seen at Baragwanath Hospital had 60 boys and 50 girls affected by Blount's disease. Birch[12] noted that boys are affected more often than girls. Inaba, Saito and Takamura[29] in their multicentre study in Japan had more females than males with Blount's disease (114 females and 76 males in the Infantile Group with 14 females and 8 males in the Adolescent Group). These results are equivocal with regards to gender influence on Blount's disease.

Bilateral involvement has been studied my many authors. Sabharwal *et al*.[22] found that bilateral deformity is more common in the Infantile Group (59% of children in the Infantile Group compared to 36% of children in the late-onset Group). Bradway *et al*.[14] noted that Blount's disease is often bilateral and symmetric in the Infantile Group whilst being unilateral in most patients with Adolescent Blount's disease. Bathfield and Beighton[11] in their series of Infantile Blount's patients had 82% of patients that exhibited changes that were bilateral and symmetrical. Inaba *et al*.[29] in their multicentre study found that the Infantile Group had a larger proportion of patients with bilateral Blount's disease (42%). Birch[12] noted that 'approximately 50% of cases are bilateral but not necessarily symmetric' in patients with Infantile Blount's disease. White *et al*.[28] had 60% of patients with evidence of bilateral involvement. The Infantile Group has an increased frequency of bilateral involvement while the late-onset Group tends to have more unilateral involvement as evidenced by the above studies.

Blount's disease has a genetic component with several reports demonstrating a possible hereditary cause for the disease but a direct pattern of inheritance has not been

demonstrated.[14,30-33] Langenskiold and Riska[30] reported four patients with Blount's disease who were members of the same family. Sibert and Bray[31] reported on a family with an autosomal dominant mode of inheritance with variable penetrance. Tobin[32] reported on a family with three affected members. Schoenecker *et al*.[34] documented a positive family history for 14 of 33 patients. Reviews by White *et al*.[28] and van Huyssteen *et al*.[33] of late-onset Blount's patients in the Western Cape did not reveal any positive family history. Bathfield and Beighton[11] noted that ten siblings had bow legs and 16 parents were similarly affected during their own infancy. These results indicate that a genetic component is associated with Blount's disease.

1.2 Literature review

Ethnicity

- Loder and Johnston[13] reported that in the USA there is an increased prevalence of Infantile Blount's disease in the African American and Hispanic population than European or Asian groups.
- Bradway *et al*.[14] found that blacks are more commonly affected than whites and the deformity is more common in the West Indies, Finland and Africa.
- Bathfield and Beighton[11] had no instances of Blount's disease in white or Indian children and all patients in their series were black African.

Genetic Inheritance

- Langenskiöld and Riska[30] reported four children with Blount's disease who were members of the same family.
- Sibert and Bray[31] reported on a family with an autosomal dominant mode of inheritance with variable penetrance.
- Tobin[32] reported on a family with 3 affected members
- Schoenecker *et al*.[34] noted a positive family history for 14 of 33 patients.

- Reviews by White *et al*.[28] and van Huyssteen *et al*.[33] of late-onset Blount's patients in the Western Cape did not reveal any positive family history.
- Bathfield and Beighton[11] noted that 10 siblings had bow legs and 16 parents were similarly affected during their own infancy.

Gender

- White *et al*.[28] reported a 2:3 male to female ratio in the late-onset Group.
- Bradway *et al*.[14] found that boys and girls were equally affected in Infantile Blount's disease
- Bathfield and Beighton[11] in their series of patients seen at Baragwanath Hospital had 60 boys and 50 girls affected by Blount's disease.
- Birch[12] noted that boys are affected more often than girls.
- Inaba *et al*.[29] in their multicentre study in Japan had more females than males with Blount's disease (114 females and 76 males in the Infantile Group with 14 females and 8 males in the Adolescent Group)

Laterality

- Sabharwal *et al*.[22] found that bilateral deformity is more common in the Infantile Group (59% of children in the Infantile Group compared to 36% of children in the late-onset Group).
- Bradway *et al*.[14] noted that Blount's disease is often bilateral and symmetric in the Infantile type whilst being unilateral in most patients with Adolescent Blount's disease.
- Bathfield and Beighton[11] in their series of Infantile Blount's patients had 82% of patients that exhibited changes that where bilateral and symmetrical.
- Inaba *et al*.[29] in their multicentre study found that the Infantile Group had a larger proportion of patients with bilateral Blount's disease (42%).
- Birch[12] noted that 'approximately 50% of cases are bilateral but not necessarily symmetric' in children with Infantile Blount's disease.

- White *et al*.[28] had 60% of patients with evidence of bilateral involvement in patients with late-onset Blount's disease.

Obesity

- Cook *et al*.[25] using finite element analysis found that obesity caused forces strong enough to retard growth in the physis.
- Davids *et al*.[26] examined gait deviations associated with obesity and found that an obese child had difficulty with hip adduction and produced the supposed 'fat-thigh gait.' This produces a varus moment on the knees and increases compressive forces across the medial part of the proximal tibia to inhibit physeal growth.
- Sabharwal *et al*.[22] found that children with Infantile Blount's disease had a more severe proximal tibial deformity compared to the Adolescent group despite their BMI being lower.
- Bathfield and Beighton[11] reported no difference with regards to early walking age or obesity in children with Blount's disease compared to unaffected children.
- White *et al*.[28] in their review of late-onset Blount's patients in Cape Town had 61% obese patients (53% juvenile and 74% adolescent).

1.3 Study Aim and Objectives

The aim of this study is to explore the profile of patients with Blount's disease seen at Chris Hani Baragwanath Academic Hospital (CHBAH). Demographic data including the age when the deformity was first noticed, age at presentation, race, gender, obesity, milestones, bilateral involvement and family history will be documented. This study will provide further information to our understanding of this disease.

CHAPTER 2

2 Methodology

2.1 Research Question

How does the profile of patients with Blount's disease seen at CHBAH compare with that seen in other populations?

2.2 Research Design

This is a hospital-based, retrospective case series with an evaluation of hospital and outpatient records (data sheets) of children diagnosed with Blount's disease (early and late-onset) from 01 January 2003 to 31 December 2016. The data was captured in an electronic spread sheet (Microsoft excel) using patient allocated numbers as identification of the entry. The following information was included in the data collection: age at onset, gender, race, weight (including whether obese or not as defined by the percentile for sex and age), milestones, bilateral involvement and family history.

2.3 Materials and Methods

This study was approved by the Human Research Ethics Committee of the University of Witwatersrand and consent was obtained from the CEO of Chris Hani Baragwanath Academic Hospital. It is a retrospective case series with an evaluation of hospital and outpatient records (data sheets) of children diagnosed with Blount's disease (early and late-onset) between 01 January 2003 and 31 December 2016.

Diagnosis in the older patients was based on the typical features of Blount's disease while the metaphyseal diaphyseal angle (MDA or angle of Drennan) was used to differentiate Infantile

Blount's disease from physiological bowing with an MDA ≤ 9 degrees suggesting physiological bowing, an MDA ≥ 16 degrees indicating Infantile Blount's disease and an MDA between 9 and 16 degrees considered indeterminate.[12] Only patients with an MDA of 16 degrees or higher were included.

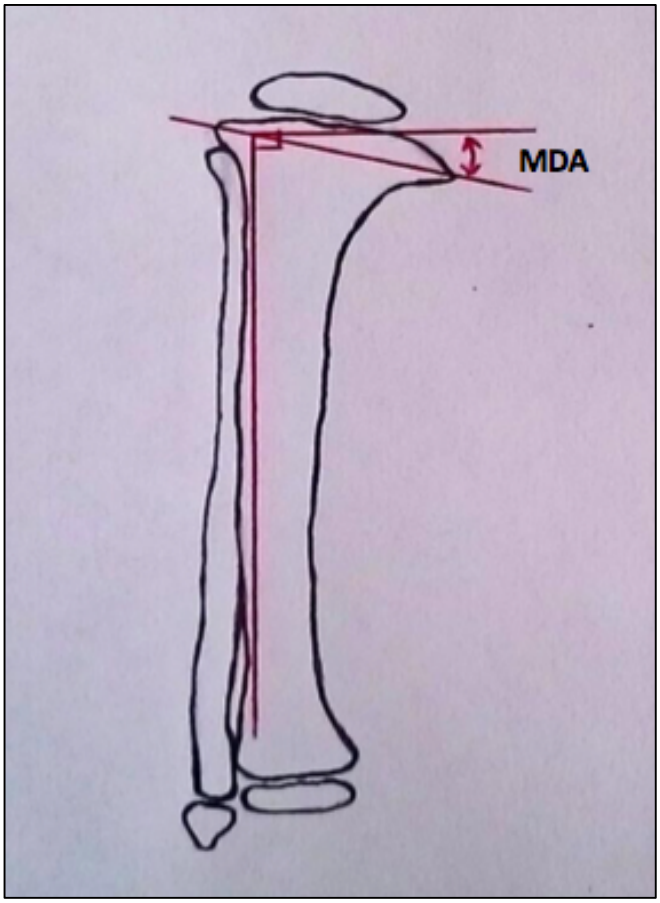

Figure 2.1 Illustration of metaphyseal diaphyseal angle (MDA or angle of Drennan) drawn by author.

The data collection form is shown as Appendix A. Demographic information including age when noticed, age at presentation, gender, race, weight, height, milestones, bilateral involvement, family history and recurrence was documented.

Patients were classified into three Groups based on age at onset of disease (recorded as age when noticed) with the Infantile Group being under four years, the Juvenile Group being four to ten years and the Adolescent Group being over 10 years.[9]

The body mass index (BMI) was obtained by dividing the weight of the patient in kilograms by the square of the patient's height in meters and is both age and gender specific.[35] The CDC BMI-for-age growth charts were used to convert the body mass index to a percentile based on a patient's age and gender. A BMI between the 5th percentile and less than the 85th percentile is considered 'normal or healthy weight,' that from the 85th percentile to less than the 95th percentile is considered 'overweight,' and that equal to or greater than the 95th percentile is 'obese'.[35]

Patients with genu varum attributable to other causes were excluded.

When the data was analysed, undocumented items were treated as missing values.

Strict confidentiality was maintained throughout the study by not recording any personal identification details.

For statistical analyses, ANOVA was done using Kruskal-Wallis rank-sum test and Dunn's post hoc test. All numerical values are presented as median with a range.

2.4 Sample

Children diagnosed with Blount's disease (early and late-onset) at CHBAH from 01 January 2003 to 31 December 2016 were included.

Patients with genu varum attributable to other causes were excluded.

Patients with missing data sheets were excluded and undocumented items were treated as missing values.

2.5 Data Collection

The relevant information was obtained from the hospital outpatient records (data sheets). The data of all the patients was stored in a database using Microsoft Excel®. Strict confidentiality was maintained throughout the study by not recording any personal identification details.

Human Research Ethics clearance and Hospital CEO approval were obtained before data collection (see Appendix B and C respectively).

2.6 Data Analysis

For statistical analyses, ANOVA was done using Kruskal-Wallis rank-sum test and Dunn's post hoc test. All numerical values are presented as median with a range.

2.7 Limitations

Major limitation of this retrospective study were the missing patient records and incompleteness of data within available patient records.

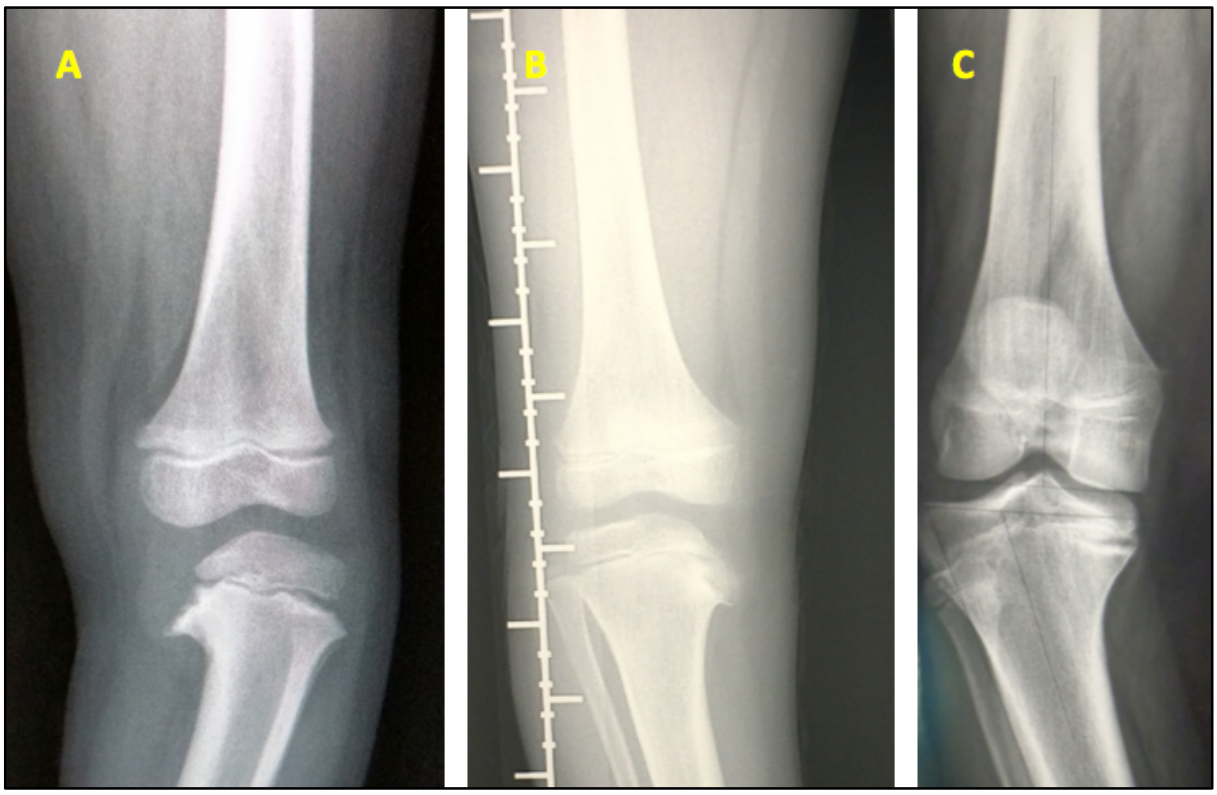

Figure 2.2 A- Three year old female with Infantile Blount's disease. B- Eight year old female with Juvenile Blount's disease. C- Eleven year old male with Adolescent Blount's disease.

CHAPTER 3

3 Results

Data was available for 108 patients with a total of 172 involved limbs. Basic demographic data is shown in Table 3.1. Table 3.2 shows the disease characteristics of patients with Blount's disease.

Table 3.1 Demographic data of patients

Variable	Total n=108	Infantile n=44	Juvenile n=36	Adolescent n=28	Chi and p values
Male %(n)	37.4 (41)	18 (8)	31 (11)	79 (22)	Chi 27.75 p<0.0001
Female %(n)	62.6(67)	82 (36)	69 (25)	21 (6)	
Age first noticed (months)	53 (12-180)	24 (12-42)	72 (53-108)	144 (126-180)	KW p<0.0001 All <0.05
Presentation age (months)	98 (18-192)	67.5 (18-156)	97.4 (62-139)	153 (123-192)	KW p<0.0001 All <0.05
Starting to sit (months)	5 (3-10) n=64	6 (3-11) n=35	5 (4-8) n=17	5 (4-9) n=12	KW p=0.3924
Starting to crawl (months)	7 (6-10) n=53	7 (6-10) n=26	6 (6-9) n=15	7 (6-10) n=12	KW p=0.3200
Starting to walk (months)	12 (8-24) n=69	12 (8-24) n=38	12 (9-15) n=19	12(8-24) n=12	KW p=0.8097
BMI median kg/m^2 (range)	24.7 (13.4-70.4) n=71	19.49 (13.4-70.4) n=33	28.5 (16.8-46.1) n=21	33.4 (17.9-64.1) n=17	KW p<0.0001 I vs J – 0.01 I vs A – 0.001 J vs A ns
Family history yes % (n)	20 (12) n=60	21.9 (7) n=32	29.4 (5) n=17	0 n=11	Chi – 3.761 p=0.1525

All numerical values are presented as median (range). ANOVA done using Kruskal-Wallis p= ANOVA result and second line indicates results of Dunn's post hoc tests. Chi^2 tests show the Chi coefficient on the first line and the p value on the second line

Table 3.2 Disease characteristics of patients with Blount's disease.

Laterality	Total n=108	Infantile n=44	Juvenile n=36	Adolescent n=28	Chi coeff (p value)
Unilateral Right/left (n)	10/34	2/14	4/13	4/7	2.124 (0.3458)
Bilateral % (n)	59.3 (64)	64 (28)	53 (19)	61 (17)	1.000 (0.6065)
Total number of limbs % (n)	79.6 (172)	81.8 (72)	76.4(55)	80.4 (45)	0.7443 (0.6893)

The Infantile Group had 44 patients (72 affected limbs), while 36 patients (55 affected limbs) had Juvenile Blount's disease, and the Adolescent Group had 28 patients (45 affected limbs). All patients in our study were of Black African ethnicity.

The Infantile and Juvenile Groups had a greater proportion of female patients while the Adolescent Group had a majority of male patients. The Infantile Group had 64% bilateral involvement while the Juvenile and Adolescent group had 53% and 61% bilateral involvement respectively. In all 3 groups with unilateral deformity, there was a predominance of left sided involvement (77%). The average age at presentation was 67.5 months (5.6 years) for the Infantile Group, 97.4 months (8.1 years) for the Juvenile Group, and 153 months (12.8 years) for the Adolescent Group. There were 12 (20%) documented cases with a family history of bow legs (7 in the Infantile Group and 5 in the Juvenile Group) while in the Adolescent Group there were no patients with a positive family history.

Data regarding sitting, crawling and walking milestones were available for 69 patients. The developmental milestones of patients within all 3 groups were within normal limits (see Table 3.1).

Data to calculate the BMI was available for 71 patients. The median (range) BMI for patients in the Infantile Group was 19.49 (13.4 − 70.4) while that for children in the Juvenile and Adolescent Groups were 28.5 (16.8 − 46.1) and 33.4 (17.9 − 64.1) respectively. Using the

CDC growth charts and based on their guidelines the Infantile, Juvenile and Adolescent Groups had a 33%, 10% and 6% overweight classification respectively (85th percentile to less than the 95th percentile) (see Table 3.3). Those patients classified as obese (≥ 95th percentile) were 42% (14 patients) in the Infantile Group, 76% (16 patients) in the Juvenile Group, and 82% (14 patients) in the Adolescent Group. When combining overweight and obese patients and comparing them to those patients with a normal BMI for age, 76%, 86% and 88% of patients had an increased BMI for age in the Infantile, Juvenile and Adolescent Groups respectively (see Table 3.4).

The median BMI was significantly higher in the male patients (33.2 (Range 16.8 − 70.4)) than in the females (22.0 (Range 13.4 − 46.1) Mann-Whitney $p < 0.0001$). Eighty two percent of male patients were classified as obese while 50% of female patients were classified as obese. There was no significant difference in the median BMI between those patients with bilateral disease (28.1 (Range 13.4 − 64.1)) and those with unilateral disease (23.9 (Range 14.0 − 70.4) Mann-Whitney $p = 0.3567$). The highest BMI recorded was that of a male patient with Infantile Blount's disease who had a BMI of 70.4.

Table 3.3 Factors affecting the proportion of overweight and obese children

Variables	**n**	**Overweight % (n)**	**Chi coeff P value**	**Obese % (n)**	**Chi coeff (p value)**
Age at onset					
Infantile	33	33 (11)	7.299	42 (14)	10.15
Juvenile	21	10 (2)	0.0260	76 (16)	(0.0063)
Adolescent	17	6 (1)		82 (14)	
Gender					
Male	27	7 (2)	3.011	82 (22)	5.764
Female	44	27 (12)	0.0827	50 (22)	(0.0164)
Laterality					
Unilateral	24	28 (7)	0.8750	52 (13)	0.0375
Bilateral	46	15 (7)	0.3496	67 (31)	(0.8464)

Comparisons for overweight and obese children were done compared to children of normal weight. All tests done were Chi ^{2} tests and present the Chi coefficient on the first line and the p value on the second line.

Table 3.4 Both overweight and obese compared to all others in the group.

Variables	**n**	**Normal BMI for age % (n)**	**↑ BMI for age (overweight + obese) % (n)**	**Chi coeff (p value)**
Age at onset				
Infantile	33	24 (8)	76 (25)	Chi 1.491 (0.4746)
Juvenile	21	14 (3)	86 (18)	
Adolescent	17	12 (2)	88 (15)	
Gender				
Male	27	11 (3)	89 (24)	Chi 1.509 (0.2192)
Female	44	23 (10)	77 (34)	
Laterality				
Unilateral	24	17 (4)	83 (20)	Chi 1.000 (ns)
Bilateral	46	17 (8)	83 (38)	

ns = not significant

CHAPTER 4

4 Discussion

Despite an increased occurrence of Blount's disease in South Africa, the aetiology is thus far unknown. Factors associated with the condition have included early walking age, large stature, obesity, race and genetics.[11,12] A total of 108 patients with 172 involved limbs was analysed. Undocumented items were treated as missing values.

All patients in this study were of Black African race consistent with a previous study by Bathfield and Beighton at the same institution in 1978 during the Apartheid era. Several studies document an increased prevalence among black populations but the reason for this association has not been elucidated.[13,14] Golding and McNeil-Smith[27] observed an increased ligamentous laxity around the knee amongst West Indian Black children and also noticed that children in this population stand and walk at an earlier age compared to European children. This combination in West Indian black children is postulated to lead to shearing forces across the medial aspect of the knee predisposing them to developing Blount's disease.

Several authors reported a possible genetic component to the disease without demonstrating a direct pattern of inheritance.[14,30-32,34] Reviews in South Africa by White *et al*.[28] and van Huyssteen *et al*.[33] did not reveal any positive family history, while Bathfield and Beighton[11] noted that 10 siblings had bow legs and 16 parents were similarly affected during their own infancy. In our study there were 12 (20%) documented cases with a family history of bow legs (7 in the Infantile Group and 5 in the Juvenile Group) while in the Adolescent Group there were no patients with a history of affected family members, thus highlighting that only in the Infantile and Juvenile Groups is a hereditary component applicable.

Early onset walking age has been proposed as a risk factor for Infantile Blount's disease and has been hypothesized to produce increased stress on the medial aspect of the proximal tibia in the predisposed infant with bow legs.[27,36] This was refuted in our study which showed a mean walking age of 13 months for the Infantile Group which is comparable to that of the general population. The gross motor developmental milestones (crawling, sitting, walking) of patients within all three Groups of Blount's disease were within normal limits.

The literature regarding gender influence for both early and late-onset Blount's disease are conflicting. With Infantile Blount's disease, some studies found boys and girls to be equally affected while other studies showed either a male or female preponderance.[11,12,14,29]

In the Infantile Group in our study we had a female predominance with a female to male ratio of 4,5:1. This contrasts with Bathfield and Beighton[11] who had slightly higher male ratio with female to male ratio of 1:1,2 in their series of Infantile Blount's patients. Inaba *et al*.[29] also had a female preponderance but the difference was much less than in our series with a female to male ratio of 1,5:1. This data suggests the possibility that different populations with Blount's disease may present differently, especially in the gender distribution as evidenced by the literature.

With regards to late-onset Blount's disease, White *et al*.[28] reported a 3:2 female to male ratio of Blount's disease which contrasts with other studies which showed a female to male ratio of 1:4. In our study we had an almost identical female to male ratio in the late-onset group, however separating this late-onset Group yielded a 2,3:1 female to male ratio in the Juvenile Group and a 1:3,7 female to male ratio in the Adolescent Group. Our study indicates that the gender preference towards female in the Juvenile Group is similar to that of the Infantile Group and that as the patients get older and into the Adolescent Group the ratio changes and male predominance occurs. There was a trend of an increasing BMI in the older male patients which will be discussed further in the BMI section of the discussion.

Several studies document an increased frequency of bilateral involvement in the Infantile Group while the late-onset Group tends to have more unilateral involvement.[11,12,14,22,29] Sabharwal *et al*.[22] found that 59% of children in the Infantile Group had bilateral deformity compared to 36% of children in the late-onset Group. Bathfield and Beighton[11] in their series of Infantile Blount's patients had 82% of patients that exhibited bilateral involvement. Inaba *et al*.[29] had 42% bilateral involvement in the Infantile Group compared to 19% of patients in the Adolescent Group. Birch[12] and Bradway *et al*.[14] found that the percentage of patients with bilateral Blount's disease was highest among the Infantile Group. Our study failed to affirm these findings with a similar occurrence of bilateral involvement in both the Infantile group (64%) and the late-onset Group (56%) (see Table 3.2). Another study from South Africa by White *et al*.[28] had 60% of patients with evidence of bilateral involvement in late-onset Blount's disease which is comparable to this study. In all three Groups of Blount's patients with unilateral involvement, there was a predominance of left sided involvement (77%). Why some patients had bilateral involvement or why the left side was predominantly affected in unilateral cases remains unexplained. This series highlights the differences in populations around the world with Blount's disease being unique from each other.

Blount's disease is documented to be associated with an increased frequency in overweight children.[9,15-17] A large percentage of patients treated with Infantile Blount's disease are greater than the 95th percentile of weight for age as reported in a number of studies in the USA.[17-21] Dietz, Gross and Kirkpatrick[17] had 67% of Blount's patients classified as obese while Raney *et al*.[19] in their series of Infantile Blount's had 63% of cases with a weight greater than the 90th percentile. Scott, Kelly and Sullivan[18] had an average BMI percentile of 97.2% in their study on Infantile Blount's disease. Sabharwal *et al*.[22] had 88% of Infantile Blount's patients and 96% of late-onset Blount's patients classified as overweight. Richards, Katz and Sims[20] had 67% while Zionts and Shean[21] had 48% of Infantile Blount's patients with a weight greater than the 95th percentile. The Heuter-Volkmann principle of asymmetric growth inhibition resulting from increased compressive forces on the medial physis can explain the pathogenesis of genu varum in Blount's disease.[22,23] The compressive forces on the medial aspect of the proximal tibia is markedly increased in obese children with genu varum.[17,24] In this study, the average BMI for patients in the Infantile group was lower than that for children in the Juvenile and Adolescent Groups (19.49 kg/m^2 compared to 28.5 kg/m^2

and 33.4 kg/m^2 respectively) (see Table 3.1), despite the Infantile Group having a more distorted epiphysis which is similar to findings by Sabharwal *et al*.[22] Patients classified as obese in our study (≥ 95th percentile) were 42% in the Infantile group, 76% in the Juvenile group, and 82% in the Adolescent Group. A significant proportion of patients (76%, 86% and 88% in the Infantile, Juvenile and Adolescent Groups respectively) had an increased BMI for age (≥ 85th percentile) (see Table 3.4). Overall a greater proportion of male patients were classified as obese compared to female patients (82% *versus* 50%) and this was statistically significant ($p = 0.0164$). There was no significant difference with the BMI of patients with unilateral and bilateral deformity. This study could not elucidate why some obese children have unilateral involvement and why some children with Blount's disease are not obese. The effect of a weight loss programme on the prognosis and natural history of Blount's disease needs to be explored with further research.[22,37]

This study is part of a series of studies at our institution related to Blount's disease adding to the volume of information on this common but poorly understood disease. The following were found to be limitations of this study: The retrospective nature of the study led to a number of missing data points for the patients enrolled in the study. Severity of disease (in terms of severity of the deformity) could not be correlated with the patients BMI. Interventional procedures were not analysed as the focus of this study was the profile of these patients.

CHAPTER 5

5 Conclusion

In this series of 108 patients (172 limbs) with Blount's disease, all patients were of Black African race and there was an unpredictable hereditary component to the disease seen in 20% of documented cases. Early-onset walking age was not a risk factor for developing Infantile Blount's disease. There was a female predominance in the Infantile and Juvenile Groups but a male predominance in the Adolescent Group. This study confirmed the documented increased frequency of bilateral involvement in the Infantile Group but showed a high incidence of bilateral involvement in the Adolescent Group too as compared with other studies. The BMI increased with increasing age and was highest in the Adolescent group. A greater number of male patients were classified as obese and this reflected the increased incidence of male gender being a risk factor in the Adolescent Group. This paper has helped to elucidate the above mentioned facts in this population of patients with Blount's disease.

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Appendices

Appendix A: Data collection form

Patient Sticker/

Name and Address

Data collection form

Genu Varum / Blounts disease

History

Surname:_____

First Names:_____

Hospital Number:_____

Date of Birth:_____ Place Of Birth:_____

Birth History:_____

Birth Weight:_____

Milestones: crawling_____ | sitting:_____| walking:_____

Family History:_____

Date of presentation/ Age: _____/_____

Height/Weight:_____/ _____ BMI $\frac{weight\ (kg)}{height^2\ (m^2)}$ _____

Infantile/Adolescent/Physiological/Rickets/Other_____

Unilateral/ Bilateral leg involvement: _____

History of main complaint:

Age when noticed_____ Photos available_____

Previous treatment received_____

_____

_____

Treating doctor/ Hospital_____

Referred from_____

Appendix B: HREC clearance certificate

R14/49 Dr M Mehtar

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M141101

NAME: (Principal Investigator)	Dr M Mehtar
DEPARTMENT:	Orthopaedic Surgery Chris Hani Baragwanath Academic Hospital Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Epidemiology of Blount's Disease seen at Chris Hani Baragwanath Academic Hospital & Charlotte Maxeke Johannesburg Academic Hospital
DATE CONSIDERED:	28/11/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr GB Firth
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	08/05/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix C: CHBAH CEO Approval Letter

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

IN THE OFFICE OF THE CEO
Enquiries: Ms. Thabile Ndlovu
Tel : (011) 933- 9145
Fax: (011) 938-1005
Email: Thabile.Ndlovu2@gauteng.gov.za

To : Dr. M Mehtar
(141101)

From : Dr. Sandile Mfenyana
CEO: CHBA hospital

Date : 24 April 2015

Re : PROFILE OF PATIENTS WITH BLOUNTS DISEASE REFERRED TO CMJAH AND CHBAH

Your application to request permission to conduct the Profile of Patients with Blount's disease referred to CHBAH and CMJAH at Chris Hani Baragwanath Academic Hospital is approved by the CEO: Dr. Sandile Mfenyana

Hoping that the Institution (CHBAH) will meet the requirements of the study concerned.

Wishing you well in your future endeavors

Regards,

DR. SCB Mfenyana
CEO: CHBA Hospital

Appendix D: PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

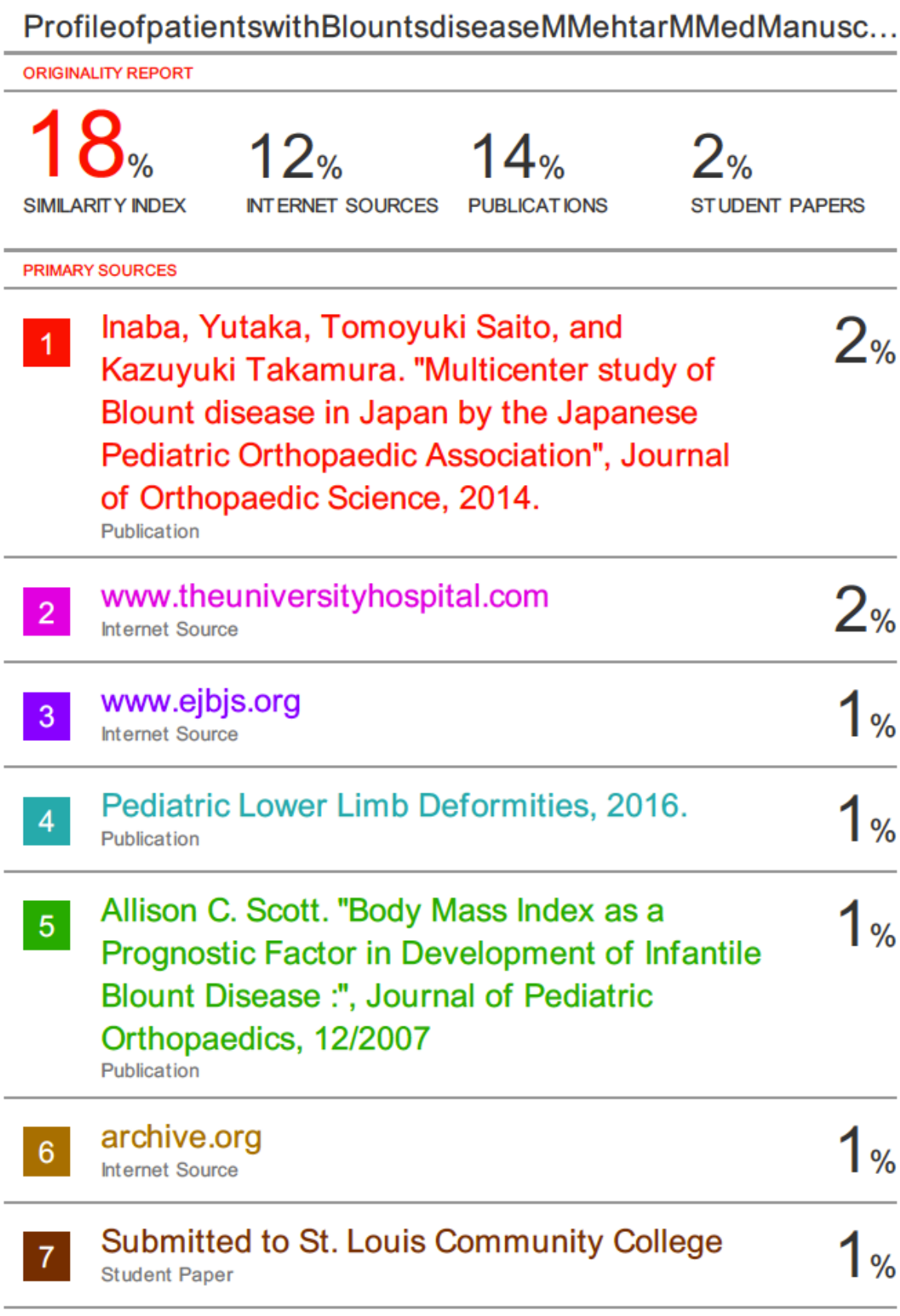
I Mohammed Mehtar (Student number: 0302629Y) am a student registered for the degree of MMed Orthopaedic Surgery in the academic year 2017.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature:  Date: 23/10/2017

Appendix E: Turn-it-in report



ProfileofpatientswithBlountsdiseaseMMehtarMMedManusc...

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