

DUANE'S RETRACTION SYNDROME IN A COHORT OF SOUTH AFRICAN CHILDREN- A 20 YEAR CLINIC BASED REVIEW

By

Dr Anna Steyn

Student nr: LRMANN001



Submitted to the University of Cape Town

In fulfilment with the requirements of the degree

MMed (Ophthalmology)

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

Supervisor: Dr Christopher Tinley, Division of Ophthalmology
University of Cape Town

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

Table of contents

Declaration	3
Abstract	4
Acknowledgements and contributions	5
Statement of contribution from co-authors	5
List of tables	6
Abbreviations	7
Chapter 2	
Published dissertation	8
Appendices	
Data capture sheet	18
Human Research Ethics approval letter	20
Departmental Research Council approval letter	21
Comments from journal reviewers	22

Declaration

I, *Anna Steyn*, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:

Signed by candidate

Date: 22/10/2019

Abstract

OBJECTIVES: To describe the clinical features of Duane's retraction syndrome in a cohort of South African children and analyse subtypes for ethnic differences.

METHODS: Retrospective case series of 120 patients seen in the period from 1997 to 2017 at the Red Cross War Memorial Children's Hospital.

RESULTS: Of the 120 patients, Type 1 was present in 76 (64%) of cases, with Type 2 in 27 (23%) and Type 3 in 16 (13%). Type 2 was most common in black children (54%), while Type 1 predominated in mixed race (68%) and white children (94%). A female predominance was seen in white children (69%) and mixed race children (59%), while there was a male predominance amongst black children (62.5%). Left involvement was the most common (44%), followed by right (41%) and bilateral involvement (14%). The average age of presentation was 2,85 years. A positive family history of squints or Duane's was present in 6 (0,5%). Congenital systemic abnormalities were present in 12 (1%) and congenital ocular abnormalities in 2 (0.4%). Squint in primary position was present in 57 (46%), of which 39% had esotropia and 61% exotropia. Squint was more common in black children (71%) than in mixed race (39.4%) and white children (41%). An abnormal head position was present in 59 (50%) and was most common in Type 2 (67%). Up and downshoots were seen in 58 (48.3%). Ametropia was found in 94 (79%), and of these 88 (93,6%) were hyperopic and 6 (6.4%) myopic. Amblyopia was present in 15 (12.5%). Surgery was performed in 41(34%).

CONCLUSION: This study is the first to provide robust data on the profile of paediatric DRS in the 3 main South African ethnic groups, and shows clear ethnic differences in DRS. In black patients, males are more often affected, the proportion with Type 2 DRS is more frequent, and surgery is required more often. Further population-based studies on the epidemiology of DRS in children are needed to clarify the role of race as a potential risk factor.

Acknowledgements and contributions

My supervisor, Dr Christopher Tinley, guided me throughout this research degree. Without him none of this would be possible. He is a co-author on the published paper and his contributions were as follows:

- Conceptualization of research question
- Assistance with structure of proposed research
- Review and editing of manuscripts

The third author, Dr Rhian Grotte also made significant contributions:

- Conceptualization of research question
- Gathering of data
- Review of manuscript

My contributions, as the candidate submitting this work for an MMed (Ophthalmology) were

- Gathering of data
- Analysis of data
- Literature review
- Writeup of manuscripts

For this reason, I am the first author in the published paper.

List of Tables

Table 1

Comparison of Epidemiological Differences Between Types of Duane's Retraction Syndrome

Page 15

Table 2

Comparison of Epidemiological Differences per Ethnicity

Page 16

Table 3 (Table A)

Previous Epidemiological Studies on Duane's Retraction Syndrome

Page 17

Abbreviations

DRS Duane's retraction syndrome

Chapter 2: Published dissertation

Published in the Journal of Pediatric Ophthalmology and Strabismus

Article Reference:

Steyn A, Grötte R, Tinley C. Duane's Retraction Syndrome in a Cohort of South African Children: A 20-Year Clinic-Based Review. JPediatr Ophthalmol Strabismus. 2019;56(4):248-253.

Duane's Retraction Syndrome in a Cohort of South African Children: A 20-Year Clinic-Based Review

Annalien Steyn, MBChB, Dip Ophth (SA); Rhian Grötte, MBBS, FRCSE, FRCOphth; Christopher Tinley, MBChB, FRCOphth (London)

ABSTRACT

Purpose: To describe the clinical features of Duane's retraction syndrome in a cohort of South African children and to analyze the differences between ethnic groups.

Methods: A retrospective case series of 120 patients seen between 1997 and 2017 at a tertiary referral center in Cape Town, South Africa.

Results: Type 2 Duane's retraction syndrome was most common in black children (54%), whereas type 1 was predominant in mixed race (68%) and white (94%) children. In this cohort, 63% of black children with Duane's retraction syndrome were boys, whereas 69% of white children and 59% of mixed race children were girls. Left eye involvement was the most common in all ethnic groups (44%), followed by right eye (41%) and bilateral (14%) involvement. The average age at presentation was 34.2 months (range: 1 to 144 months). Strabismus in primary position was present in 57 patients (46%), of whom 39% had esotropia and 61% had exotropia. A deviation in the primary position was more common in black (71%) children than in mixed race (39%) or white (41%) children. Ametropia was found in 94 patients (79%), amblyopia was present in 15 patients (13%), and 41 patients (34%) underwent surgery.

Conclusions: This is the first study to provide robust data on the profile of pediatric Duane's retraction syndrome in the three main ethnic groups in South Africa, and it showed clear ethnic differences. Among black children, boys are affected more often, the proportion with type 2 Duane's retraction syndrome is more frequent, and surgery is required more often. Among white and mixed race children, girls are affected more often and type 1 Duane's retraction syndrome is predominant.

INTRODUCTION

Duane's retraction syndrome is a congenital cranial disinnervation disorder. Its characteristic findings include a variety of horizontal motility deficits, accompanied by globe retraction and palpebral fissure narrowing on attempted adduction. It comprises between 1% and 5% of all strabismus syndromes.^{1,2} Duane's retraction syndrome is classically reported as a sporadic syndrome, with a left-sided and female predominance.³

Various classifications of Duane's retraction syndrome have been suggested,² and the most commonly used is the Huber classification based on electromyogram findings.⁴ This classification divides Duane's retraction syndrome into type 1 (marked limitation of abduction), type 2 (marked limitation of adduction), and type 3 (limitation of both abduction and adduction).

The epidemiology of Duane's retraction syndrome seems to vary according to geographical and genetic factors. DeRespinis et al.³ published the first epidemiological data on Duane's retraction syndrome in Americans, and found a 58% female majority, with type 1 being the most common (78%), followed by type 3 (15%) and type 2 (7%). A French study also found a female preponderance and type 1 to be most common.⁵ However, in a previous study of 75 South African black children, the majority of children with Duane's retraction syndrome were boys (68%) and type 2 was the most common.⁶

Most reports have emanated from studies on largely white populations in North America and

Europe.^{1-3,5,6} Little is known about the distribution and etiology of Duane's retraction syndrome in children of other ethnic groups and, in particular, data from Africa is sparse. Therefore, the aim of this study was to review all cases of Duane's retraction syndrome presenting to a tertiary pediatric eye clinic in South Africa during a 20-year period.

PATIENTS AND METHODS

This study was a retrospective, descriptive case series in which the records of all patients diagnosed as having Duane's retraction syndrome at the Red Cross War Memorial Children's Hospital between 1997 and 2017 were reviewed. Patients with incomplete data were excluded. Ethical approval was obtained from University of Cape Town's Institutional Review Board and the research followed the tenets of the Declaration of Helsinki.

The Red Cross War Memorial Children's Hospital in Cape Town, South Africa, is a large, government-administered, tertiary pediatric referral center that treats children younger than 13 years. The hospital serves the populations from the Western (6.3 million) and Northern (1.2 million) Cape Provinces.⁷ The ethnic distributions in the Western and Northern Capes are similar, with approximately 50% mixed race, 30% black, and 20% white.⁷ The majority of patients seen at our hospital are of mixed race or black ethnicity. White children and other ethnic groups often have health insurance and are largely managed within the private sector.⁸

Our mixed race group is heterogeneous with two distinct origins. The first group is made up of descendants of early intermarriages between European settlers and black natives. The second group (the Cape Malays) has historical and genetic ties with ancestors from South-East Asia. For economic reasons, the black population has gradually migrated to the western Cape and belongs mainly to the Xhosa-speaking tribe.⁹

All patients with Duane's retraction syndrome were referred by local primary health care providers, general practitioners, or hospital pediatricians. They were evaluated by a consultant pediatric ophthalmologist. During evaluation, each child underwent a comprehensive medical history and ocular and orthoptic examination. Data collected included age at presentation, presence of a family history of strabismus, any associated congenital or ocular abnormalities, type and laterality of Duane's retraction syndrome, deviation in primary position, abnormal head posturing, presence of up or down shoots, visual acuity, refraction, presence of amblyopia, whether surgery was performed, and the type of surgery.

A Pearson chi-square test was used to determine if there were any statistically significant differences between proportions and ethnicity.

RESULTS

A total of 120 patients were identified during the 20-year study period. Eighty patients were mixed race, 24 were black, and 16 were white.

In our group, 65 (54%) were female. Type 1 was the most common (63%), followed by type 2 (22%) and type 3 (15%). Left eye involvement was slightly more common than right eye involvement (46% vs 40%, respectively). Bilateral involvement was present in 14%.

The average age at presentation was 34.2 months (range: 1 to 144 months). Five patients (4.2%) had a positive family history of strabismus and 1 patient (0.8%) had a family history of Duane's retraction syndrome. One patient was a twin and the other twin did not have Duane's retraction syndrome.

Twelve patients (1%) had associated congenital systemic abnormalities: 5 Goldenhar's syndrome, 4 congenital heart defects (2 of these had esophageal atresia together with the congenital heart defects), 3 cleft palate, 1 club foot, 1 dysmorphism, and 1 hydrocephalus.

Ocular examination revealed a deviation in primary gaze in 53 patients (43%). Subset analysis showed a deviation in primary gaze mainly in type 2 (74%), followed by type 3 (56%) and then type 1 (37%). Esotropias comprised 42% of patients (22 of 53), whereas exotropias comprised 58% of

patients (31 of 53). All of the patients with esotropia had type 1 Duane's retraction syndrome. The distribution of patients with exotropia was 20 patients with type 2 (57%) and 11 patients with type 3 (26%).

Data regarding abnormal head position, presence of up and down shoots, refractive errors, and amblyopia, as present in different types, are shown in **Table 1**. A total of 41 patients (34%) underwent surgery. The indications for surgery were a deviation in primary gaze, abnormal head posture, and up or down shoots. Two patients required a second surgical procedure.

Bilateral cases were predominantly male (59%), with an incidence of deviation in primary gaze of 82% of patients (14 of 17). Surgery was required in 59% of patients (10 of 17).

Subset analysis revealed variation between children of different ethnic groups (**Table 2**). In our black children, males were more common ($P = .22$), type 2 was most prevalent ($P = .043$), and surgery was required more frequently ($P = .009$).

DISCUSSION

Several epidemiological studies show a marked variation in the clinical features of Duane's retraction syndrome worldwide. These studies are summarized in **Table A** (available in the online version of this article).^{3,6,10-19}

The results from our cohort corroborate findings from a previous study of black South African children with a male preponderance for Duane's retraction syndrome.⁶ Young⁶ primarily researched the Zulu ethnic group. The Zulu group has close ties to the Xhosa-speaking tribes, and they have similar origins in the Nguni people. The Nguni are said to have migrated to the Great Lakes region from North Africa before continuing on down south. Due to their common origin, their languages and cultures show marked similarities.⁹ Zang¹⁰ and Park et al.¹¹ found an equal incidence of males and females of Asian descent in China and Korea. All other reports show a female predominance ranging from 55% to 63%.¹²⁻¹⁹

In most reports, type 1 is the most common, followed by type 3 and then type 2.²⁻⁴ In our series, type 1 was the most common (62%), but there were more patients with type 2 (23%) than type 3 (15%). However, our type distribution showed ethnic differences. In our black population, type 2 was the most common (54%), followed by type 1 (33%) and type 3 (14%). These results are also aligned with Young's study of black South African children⁶ because her results showed a majority of type 2 (58%), followed by type 1 (33%) and then type 3 (9%). No other epidemiological studies have found a type 2 majority. In our mixed race population, there was a large majority of type 1 (68%), whereas type 2 (17%) was slightly more common than type 3 (15%). This may be a reflection of their South-East Asian descent, because other studies from South-East Asian populations showed comparable results. Shrestha and Sharma¹⁵ showed that in Nepal, type 1 is most common by a large margin (73%) and that type 2 (15%) is more common than type 3 (12%). Sarfraz et al.¹⁹ showed similar results in patients from Pakistan (68%, 20%, and 10%) and Anvari et al.¹³ showed the same pattern in Iran (87%, 6.5%, and 5.7%).

In our study, bilateral cases of Duane's retraction syndrome comprised 10% in mixed race children, 21% in black children, and 25% in white children. The mixed race findings are in keeping with the 12% bilaterally in India reported by Mohan et al.¹⁴ and Kekunnaya et al.,¹⁶ as well as the 14% reported by Khan et al.¹² in Saudi Arabia and Shawky et al.¹⁷ in Egypt. The 21% prevalence of bilateral cases in our black population is in keeping with the findings of Young,⁶ in which a higher incidence of bilateral cases (33%) was present among black South Africans. Although our numbers were small, we had a high incidence of bilateral cases in our white patients (25%) and Mehel et al.¹⁸ in France found the incidence of bilateral disease in their series to be 21.7%.

The average age of presentation varies world-wide from 10 months to 13.84 years, with no statistical difference in the time of presentation of different subtypes.^{11,14,16} In our setting, the average age at presentation was 34.2 months, with no significant difference in the age of

presentation of the different subtypes.

Family history was present in 0.05% in our series. Other series showed that a positive family history for Duane's retraction syndrome and/or strabismus ranges from 0.03% to 10%.^{4,7,16,19} Sevel and Kasser²⁰ reported three successive generations in South Africa with bilateral Duane's retraction syndrome, suggesting an autosomal dominant inheritance in that family. No other studies describe a heritable mode of transmission of Duane's retraction syndrome and our series supports this notion.²¹ Congenital systemic abnormalities were present in 1% of patients, whereas congenital ocular abnormalities were present in 0.4% of patients. All of the observed systemic and ocular associations in our patients have been described previously.^{21,22} Zhang¹⁰ and Park et al.¹¹ found a 12% incidence of crocodile tears, whereas Kekunnaya et al.¹⁶ found cataract to be their most common ocular association.

Refractive error in the current study was predominantly hypermetropia (74%), with myopia being much less common (0.05%). Hypermetropia is reported to be present in 30% to 80% of patients with Duane's retraction syndrome.²¹

Amblyopia was found in 12.5% of patients in our study. In other research, amblyopia was documented in 3% to 25% of cases.^{16,23,24} There was no difference in the incidence of amblyopia according to types and laterality, and this is in keeping with previous reports.

A horizontal deviation in primary position was present in 46% of our cases, with bilateral Duane's retraction syndrome being the most common (82.4%), followed by type 2, type 3, and then type 1 (74%, 56%, and 37%). There are marked geographical differences in the incidence of horizontal deviation in primary gaze in Duane's retraction syndrome, with reports varying from 13.6% to 90.2%.^{11,13-16,19} The higher incidence of horizontal strabismus in bilateral cases (82% vs 44%) is in keeping with the findings of Mohan et al.,¹⁴ Khan and Oystreck,²⁵ and Zanin et al.,²⁶ whereas Kekunnaya et al.¹⁶ reported an equal incidence in horizontal strabismus in unilateral and bilateral cases. Only O'Malley et al.²⁷ reported a higher incidence in unilateral cases.

Vertical deviations in the form of up or down shoots were present in 48% of our cases. The incidence of vertical deviations ranges from 12.8% to 61%.^{10,11,13,16,19} We found vertical deviations were most common in type 3 (81%), followed by type 2 (70%) and then type 1 (34%). Kekunnaya et al. also found an 80% incidence of up and down shoots in type 3.¹⁶

An abnormal head posture was found in 50% of cases. This ranges in the literature from 16.7% to 76%.^{10-11,13,16,18,19} Type 2 had significantly more face turn than type 1 or type 3 and this contrasts with the findings of Kekunnaya et al., where a face turn was significantly less common in type 2.¹⁶

Surgery was performed in 34% of cases. Analyzed by subset, type 3 required surgery most often (69%), followed by types 2 (29%) and 1 (29%). Previous reports showed with statistical significance that patients with type 2 Duane's retraction syndrome required surgery more frequently.^{16,19,27} In the current study, patients with type 3 required surgery most often, and all surgeries for type 3 were at least partially indicated by the presence of up or down shoots (81%).

Limitations of this study largely surround its retrospective, clinic-based design. Incidence rates of Duane's retraction syndrome cannot be inferred because it is not population-based. It is possible that a proportion of the children with Duane's retraction syndrome within the population served by our institution did not present to the clinic and were therefore not included. Unavoidable inaccuracies arose in history-taking due to language barriers, and we relied on caregivers' recollections of the onset of deviation, without the aid of photographs. Nevertheless, this study is the first to provide robust data on the profile of pediatric Duane's retraction syndrome in the three main South African ethnic groups. We found clear ethnic differences in Duane's syndrome in our cohort.

In black children, boys are more commonly affected than girls, the incidence of type 2 Duane's retraction syndrome is more frequent than types 1 and 3, and surgery is required more often. In mixed race children, type 2 is more common than type 3. In mixed race and white children, females and type 1 predominate, following North American and European trends. Further population-based

studies on the epidemiology of Duane's retraction syndrome in children are needed to clarify the role of race as a potential risk factor.

REFERENCES

1. Gurwood AS, Terringo CA. Duane's retraction syndrome: literature review. *Optometry*. 2000;71:722-726.
2. Kekunnaya R, Negaalur M. Duane retraction syndrome: causes, effects and management strategies. *Clin Ophthalmol*. 2017;11:1917-1930.
3. DeRespinis PA, Caputo AR, Wagner RS, Guo S. Duane's retraction syndrome. *Surv Ophthalmol*. 1993;38:257-288. Erratum in: *Surv Ophthalmol*. 1996;40:423.
4. Huber A. Electrophysiology of the retraction syndromes. *Br J Ophthalmol*. 1974;58:293-300.
5. Zanin E, Gambarelli N, Denis D. Distinctive clinical features of bilateral Duane retraction syndrome. *J AAPOS*. 2010;14:293-297.
6. Young S. Characteristics of Duane's retraction syndrome at a clinic in South Africa. *Surv Ophthalmol*. 1997;42:295.
7. Lehohla P. Census 2011: census in brief. Pretoria, South Africa: Statistics South Africa; 2012. http://www.statssa.gov.za/census/census_2011/census_products/Census_2011_Census_in_brief.pdf
8. Lalloo R, Myburgh NG, Smith MJ, Solanki GC. Access to health care in South Africa: the influence of race and class. *S Afr Med J*. 2004;94:639-642.
9. Beck RB. *The History of South Africa*, 2nd ed. Santa Barbara, CA: Greenwood; 2014.
10. Zhang F. Clinical features of 201 cases with Duane's retraction syndrome. *Chin Med J (Engl)*. 1997;110:789-791.
11. Park WH, Son DH, Yoon SW, Baek SH, Kong SM. The clinical features of Korean patients with Duane's retraction syndrome. *Korean J Ophthalmol*. 2005;19:132-135.
12. Khan AO, Oystreck DT, Wilken K, Akbar F. Duane's retraction syndrome on the Arabian Peninsula. *Strabismus*. 2007;15:205-208.
13. Anvari F, Hatef E, Mohammadi SF, Eskandari A. Duane's retraction syndrome, a case series from Iran. *Int Ophthalmol*. 2008;28:275-280.
14. Mohan K, Sharma A, Pandav SS. Differences in epidemiological and clinical characteristics between various types of Duane retraction syndrome in 331 patients. *J AAPOS*. 2008;12:567-580.
15. Shrestha GS, Sharma AK. Duane's retraction syndrome: a retrospective review from Kathmandu, Nepal. *Clin Exp Optom*. 2012;95:19-27.
16. Kekunnaya R, Gupta A, Sachdeva V, et al. Duane retraction syndrome: series of 441 cases. *J Pediatr Ophthalmol Strabismus*. 2012;49:164-169.
17. Shawky D, Gaballa K, El Basha M. Duane retraction syndrome, Egyptian study. *Adv Ophthalmol Vis Syst*. 2015;3:00089.
18. Mehel E, Quere MA, Lafenant F, Pechereau A. Epidemiological and clinical aspects of Stilling-Turk-Duane syndrome [article in French]. *J Fr Ophthalmol*. 1996;19:533-542.
19. Sarfraz S, Nuzhat S, Khan A. Duane's syndrome: surgical outcome and non-ophthalmologic associations. *J Ayub Med Coll Abbottabad*. 2014;26:328-330.
20. Sevel D, Kassir BS. Bilateral Duane syndrome: occurrence in three successive generations. *Arch Ophthalmol*. 1974;91:492-494.
21. Kekunnaya R, Negaalur M. Duane retraction syndrome: causes, effects and management strategies. *Clin Ophthalmol*. 2017;11:1917-1930.
22. Assaf AA. Congenital innervation dysgenesis syndrome (CID)/ congenital cranial disinnervation disorders (CCDDs). *Eye (Lond)*. 2001;25:1251-1261.
23. Tredici TD, van Noorden GK. Are anisometropia and amblyopia common in Duane's syndrome? *J Pediatr Ophthalmol Strabismus*. 1985;22:23-25.

24. Kirkham TH. Anisometropia and amblyopia in Duane's syndrome. *Am J Ophthalmol*. 1970;69:774-777.
25. Khan AO, Oystreck D. Clinical characteristics of bilateral Duane syndrome. *J AAPOS*. 2006;10:198-201.
26. Zanin E, Gambarelli N, Denis D. Distinctive clinical features of bilateral Duane retraction syndrome. *J AAPOS*. 2010;14:293-297.
27. O'Malley ER, Helveston EM, Ellis FD. Duane's retraction syndrome-plus. *J Pediatr Ophthalmol Strabismus*. 1982;19:161-165.

Table 1

TABLE 1 Comparison of Epidemiological Differences Between Types of Duane's Retraction Syndrome			
Characteristic	Type 1	Type 2	Type 3
No.	75	27	18
Age (months)	39.9	29.7	33.9
Male	28 (37%)	18 (67%)	8 (44%)
Female	47 (63%)	9 (33%)	10 (56%)
Right eye	27 (36%)	10 (37%)	11 (61%)
Left eye	36 (48%)	14 (52%)	5 (28%)
Bilateral	12 (16%)	3 (11%)	2 (11%)
Esotropia	22 (29%)	0	0
Exotropia	0	20 (74%)	11 (61%)
Hypermetropia	44 (59%)	19 (70%)	13 (72%)
Myopia	1 (1%)	2 (7%)	3 (17%)
Amblyopia	10 (13%)	3 (1%)	2 (11%)
Face turn	32 (43%)	18 (67%)	9 (50%)
Up or down shoots	25 (33%)	19 (70%)	15 (83%)
Surgery	22 (29%)	8 (30%)	11 (61%)

Table 2

TABLE 2 Comparison of Epidemiological Differences per Ethnicity			
Characteristic	Black	Mixed Race	White
No.	24	81	16
Male:Female	62.5%	41%	31%
Type 1	33%	68%	94%
Type 2	54%	17%	6%
Type 3	14%	15%	0%
Right:Left	29%	47%	25%
Bilateral	21%	10%	25%
Deviation in primary position	71%	39.5%	44%
Exotropia	82%	60%	14%
Esotropia	18%	40%	86%
Abnormal head posture	58%	51%	38%
Surgery	33%	15%	37.5%

Table A

Country	South Africa	South Africa	USA	China	Korea	Saudi Arabia	Iran	India	Nepal	India	Egypt	France	Pakistan
Author	Steyn	Young ⁶	DeRespinis ⁴	Zang ¹⁰	Park ¹¹	Khan ¹²	Anvari ¹³	Mohan ¹⁴	Shresta ¹⁵	Kekhunnaya ¹⁶	Shawky ¹⁷	Mehel ¹⁸	Sarfraz ¹⁹
Date	2018	1997	1993	1997	2005	2007	2005	2008	2012	2012	2015	1996	2014
Number	120	75	–	201	78	404	128	331	41	441	198	155	41
Bilat %	14	33	18	–	3	14	7	12	5	12	14	21	2
Left eye %	45	35	59	66	83	–	78	65	68	68	58	72	66
Right eye %	41	31	23	–	14	–	22	23	27	20	28	7	23
Females %	54	32.5	58	50	51	55	60	60	58.5	52	48	54	63
Males %	46	67.5	42	50	49	45	40	40	41.5	48	52	46	37
Type 1 %	62.5	33	78	91.5	86	78	87	73	73	83	73	–	68
Type 2 %	22.5	58	7	–	2	4	7	4	15	2	5	–	20
Type 3 %	15	9	15	–	12	19	6	11	12	3	22	–	10
Deviation in primary %	44	–	–	–	41	–	14	65	59	65	–	–	90
AHP %	49	–	–	40	16.7	–	71	–	–	60	–	65	76
Shoots %	49	–	–	20	15	–	13	–	24	48	–	–	61
Surgery %	34	–	–	–	40	–	71	–	–	–	47	–	63
Amblyopia %	13	–	–	–	5	27	27	10	–	10	15	33	–
Systemic abn %	1	–	–	–	–	–	–	6	–	3	–	11	15
Ocular abn %	0.4	–	–	12	–	–	–	12	–	8	–	14	–
Fam hx %	0.5	–	10	–	–	–	–	–	–	8	–	6	–

Bilat = bilateral; AHP = abnormal head posture; abn = abnormalities; fam hx = family history

Appendix 1: Data Capture sheet

Name			
Hospital Number			
Race			
Sex			
Date of Birth			
Age at presentation			
Twin	Yes	No	
Family history			
Congenital abnormalities			
Ocular abnormalities			
Type of Duane's			
Laterality	Right	Left	Bilateral
Deviation in primary			
Abnormal head posture	Yes	No	
Upshoot/Downshoot			
Visual Acuity	Right	Left	

Refraction	Right	Left
Amblyopia	Yes	No
Surgery	Yes	No
Indications for surgery		
Comments		

Appendix 2: Human Research Ethics approval letter



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



Room E53-46 Old Main Building
Grootes Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

06 August 2018

HREC REF: 476/2018

Dr Chris Tinley
Ophthalmology
H53, OMB

Dear Dr Tinley

PROJECT TITLE: DUANE SYNDROME IN SOUTH AFRICAN BLACK AND MIXED-RACE CHILDREN - A 20 YEAR CLINIC-BASED REVIEW (MMED CANDIDATE - DR A STEYN)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned.

- Please close study 137/2013 by completing the FHS010 form.

Approval is granted for one year until the 30 August 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate Institutional approval, where necessary, before the research may occur.

The HREC acknowledge that the student, Dr Anna Steyn will also be involved in this study.

Yours sincerely

Signature removed to avoid signature online

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 476/2018

Appendix 3: Departmental Research Council Approval



UNIVERSITY OF CAPE TOWN



Department of Surgery
Departmental Research Committee
Dr Timothy Pennel
D24 Office, Groote Schuur Hospital
Observatory 7925
South Africa
Tel (021) 404 3430
Email: tim.pennel@uct.ac.za

15 May 2018

Dr A Steyn
Department of Surgery
University of Cape Town

Dear Dr Steyn

RE: Project 2018/044

PROJECT TITLE: Duane Syndrome In South African Black And Mixed Race Children – A 20 Year Clinic-Based Review

The above protocol has been reviewed by the Department of Surgery Research Committee. I am pleased to inform you that the committee approved the scientific merit of the study, and endorse the protocol for submission to the relevant ethics committee.

Although this letter serves as confirmation that the above protocol has successfully passed through the surgical DRC, respective ethics committees still require DRC chair signature before submission.

Please use the above project number in all future correspondence,

Yours sincerely

Signature removed to avoid exposure online

DR TIMOTHY PENNEL
CHAIRMAN: RESEARCH COMMITTEE

Appendix 4: comments from journal reviewers

Dear Dr Steyn,

Your manuscript entitled, "Duane's Retraction Syndrome in a cohort of South African children - a 20-year clinic-based review" (JPOS-2019-031), has been provisionally accepted for publication in the Journal of Pediatric Ophthalmology & Strabismus, pending certain revisions. The attached comments, made by the Editorial Board, should assist you.

To submit your revision, please go to <https://www.editorialmanager.com/jpos/> and login as an Author. You will find your manuscript in the "Submissions Needing Revision" folder.

When you submit the revised manuscript, please outline in your Response to Reviewers the specific changes you made (and where they can be found in the manuscript). Your revised manuscript must be returned within 30 days of this letter.

Please also remember not to embed images in the Word file; the journal requires individual TIFF or JPEG files to be uploaded for each image.

In accordance with the International Committee of Medical Journal Editors' (ICMJE) guidelines, all authors are required to complete and submit the ICMJE Form for Disclosure of Potential Conflicts of Interest. This form is found at <https://www.healio.com/ophthalmology/journals/jpos/submit-an-article>, and must be uploaded for each author at the time of manuscript resubmission, if not previously submitted. Completion of this form for each author is required prior to acceptance of any manuscript.

Per journal policy, final manuscript acceptance is contingent upon successfully passing a plagiarism software check.

Thank you for your interest in the Journal of Pediatric Ophthalmology & Strabismus.

Sincerely,
Rudolph S. Wagner, MD
Editor

Reviewers' comments:

Remember that the article will not be considered for final acceptance until we have copyright/disclosure forms from all authors.

Reviewer #1: Well written and interesting. Should you have mentioned Kassari's article out of Groote Schuur in the 1970's?

Reviewer #2: This article discusses Duane syndrome in South Africa over two decades. It does add to the literature in regards to the different statistics based on race.

A few comments, throughout the paper it says left or right at times instead of left eye or right eye

Also many numbers have a comma instead of a period

The writing is in the English style of the UK, not the United States for spelling of many words

Coloured should be removed in describing a group

In the US we use strabismus instead of squint