Blood management strategies in posterior corrective surgery for idiopathic scoliosis

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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

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Declaration

I *Mohammad Hamza Sultan Aftab* 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.

………………………
(Signature of candidate)

26th day of November 2022 in Johannesburg.

Dedication

Dedicated to my wife, Javeria, for her devotion and her unconditional support of both my professional and academic pursuits.

Secondly dedicated to my parents, Aftab and Ayesha Younus, for their love and pushing me to aspire to greatness.

Presentations arising from the research project

1. *"Blood management strategies in posterior corrective surgery for idiopathic scoliosis"* – Presented at the 68th Congress of the South African Orthopaedic Association - 5-8 September 2022
2. *"Blood management strategies in posterior corrective surgery for idiopathic scoliosis"* – Presented at the Second Annual Wits Orthopaedic Surgery Research Day – 9 November 2022

Abstract

Background:

Corrective surgery for idiopathic scoliosis is associated with large volumes of blood loss and a need for blood transfusion. The aim of the study was to measure blood loss and blood products used intra-operatively in corrective surgery, and to identify modifiable factors that may influence blood loss.

Methods:

The study was a retrospective review of patients who underwent posterior corrective surgery for idiopathic scoliosis between 2015 and 2020. A total of 43 patients were identified, of which 36 met the inclusion criteria. Sociodemographic data, intra-operative blood loss parameters, transfusion requirements, and use of tranexamic acid, intra-operative cell salvage and ultrasonic bone scalpel were documented. Data were analysed to identify factors affecting intra-operative blood loss and blood transfusion.

Results:

The 36 patients (30 female, 6 male) had a median age of 16 (interquartile range: 13-17) years. The mean duration of surgery was 355 (+/-75.38) minutes and the average number of segments fused was 10.25 (+/- 1.87). The mean estimated blood loss was 722.22 (+/-328.30) mL with the mean percentage blood loss being 22.99 (+/-11.61) %. A total of 11 patients (30.56%) received a blood transfusion; in these patients every 139.58 mL of blood lost resulted in 1 unit of blood being transfused (p=0.005). Statistically significant differences in mean estimated blood loss were found with the use of tranexamic acid (p=0.018) and ultrasonic bone scalpel (p=0.01). The use of intra-operative cell salvage did not result in statistically significant differences in mean estimated blood loss. A direct correlation was also found with estimated blood loss and the duration of surgery (p=0.025), and the number of segments fused (p=0.005).

Conclusion:

Modifiable factors affecting intra-operative blood loss include the use of tranexamic acid, ultrasonic bone scalpel, duration of surgery and the number of segments fused. A multifactorial blood management strategy should be implemented to decrease blood loss and reduce the need for blood transfusion in corrective scoliosis surgery.

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Nomenclature

AIS	Adolescent Idiopathic Scoliosis
CHBAH	Chris Hani Baragwanath Academic Hospital
COVID-19	Coronavirus Disease
EBL	Estimated Blood Loss
EBV	Estimated Blood Volume
g/dL	Grams per decilitre
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
ICS	Intra-operative Cell Salvage
IQR	Interquartile Range
Kg	Kilogram
L	Litre
MAC	Medical Advisory Committee
mg/kg	Milligrams per kilogram
mg/kg/h	Milligrams per kilogram per hour
mL	Millilitre
mL/kg	Millilitre per kilogram
PMTSS	Predictive Model of Transfusion in Spine Surgery
RBC	Red Blood Cell
RCT	Randomised Control Trial
SD	Standard Deviation
TXA	Tranexamic Acid
UBS	Ultrasonic Bone Scalpel

Chapter 1

Introduction and literature review

1.1 Background

Scoliosis is an abnormal rotational deformity of the spine, ranging in severity from being exclusively cosmetic to causing life-threatening respiratory compromise. Scoliosis which has no identifiable cause is termed idiopathic scoliosis (1, 2). Idiopathic scoliosis can be further classified into three subtypes according to the age of onset. These subtypes are infantile (from birth to 3 years), juvenile (3-10 years), and adolescent (after 10 years) (3). Corrective spine surgery for the treatment of scoliosis is thus aimed at halting the progression of the deformity and restoring the normal contours of the spine with instrumentation (1). With advances in spine surgery, the number of spine procedures performed has risen substantially, with recent increases reported to be more than 200% compared to the 1990s (4).

Scoliosis surgery often requires extensive soft tissue dissection, bone cutting and lengthy operative times. These procedures are frequently associated with large volumes of perioperative blood loss, with reported losses up to approximately 4.5L (5-7). This blood loss subsequently leads to an elevated incidence of allogeneic blood transfusion, with transfusion rates being as high as 59% in children undergoing scoliosis surgery and between 16-81% in adults undergoing spine surgery (5, 8).

In a developing country such as South Africa which has limited funds and resources, any intervention that has the potential to decrease healthcare cost and morbidity needs to be investigated and instituted. Therefore, with the increase in frequency of spine procedures, including for idiopathic scoliosis (4, 9), identification of factors affecting blood loss and transfusions with the implementation of blood management strategies is crucial. Furthermore, while a large quantity of data is available regarding blood loss in spine surgery internationally, there is none that originates in South Africa.

1.2 Literature Review

1.2.1 Allogeneic Blood Transfusions

Allogeneic blood transfusions are unfortunately not without considerable risk and cost; consequently, it is reserved for clinically significant blood loss. Thus, as the quantity and complexity of scoliosis cases increase, blood loss and its management in scoliosis surgery becomes a focal topic (4, 10). South Africa already possesses a large burden of disease caused by Human Immunodeficiency Virus (HIV) and tuberculosis. Additionally, it has severely limited funds available for healthcare and cannot afford further burdens of disease caused by complications related to blood loss and transfusions.

The implementation of allogeneic blood transfusion in spine surgery (whilst limited to cases with clinically relevant blood losses) is accompanied by a multitude of potential problems. Blood transfusions are known to be associated with several serious complications, including transmission of blood borne viruses, transfusion-related acute lung injury, acute haemolytic reactions, and transfusion-induced immunomodulation (4-6). Blood borne viruses such as HIV and Hepatitis B and C are commonly implicated and are a cause for health concern. However, their transmission through this route has decreased with improvements in testing (5, 6). Complications related to transfusions of greatest concern are those caused by circulatory fluid shifts; severely injuring the heart, lungs, and kidney, causing volume overload, transfusion-related acute lung injury, and acute kidney injury (4). Additionally, transfusion induced immunomodulation is implicated in a higher incidence of post-operative nosocomial infections, adding to patient morbidity (5, 6). Retrospective reviews have shown that post-operative transfusions lead to increased complications, extended hospital stays, greater patient mortality, and increased healthcare costs (4, 6, 11).

Allogeneic red blood cells (RBCs) used for transfusion are a scarce resource and therefore can be an expensive form to treat blood loss. Consequently, blood products often contribute substantially to the total healthcare costs (12). The South African National Blood Service reported the cost for one unit of RBC concentrate for state and private patients (for the period 2021- 2022), to be R 2158.17 and R 2787.35, respectively (13). It is important to note that this cost excludes other indirect costs related to transfusions. For instance, costs of crossmatching blood and packaging. In a developing country such as South Africa, this fundamentally leads to substantially increased cost and causes the already limited financial resources to be diverted away from other essential services and medication. In scoliosis surgery where large blood losses are anticipated, it is incumbent upon the treating doctor to carefully balance the risk/cost to benefit of blood transfusions (12).

1.2.2 Risk Factors for Blood Loss in Scoliosis Surgery

Guidelines that promote minimising blood loss act on the principle of preventative medicine. Preventative medicine aims to prevent pre- and post-operative complications and therefore aim to decrease healthcare costs (8). In the desire to establish these guidelines, various factors have been identified that lead to increased blood losses in scoliosis surgery. These factors can generally be separated into patient and surgery-related factors, to identify modifiable factors that influence blood loss (14).

The identification of these modifiable factors continues to remain the priority concern of recent research (14). Patient factors postulated to influence blood losses include: advanced age, elevated body mass index, pre-existing medical conditions, and medication. Whilst surgery-related factors include: greater surgical complexity, prolonged operative time, surgical haemostasis, and longer fusion constructs (4, 8, 14, 15). Additionally, the pre-operative degree of kyphosis and Cobb angle (i.e. the magnitude of the main curve) are variables that have been demonstrated to also influence intra-operative blood loss (14, 16).

These factors were investigated by Lenoir et al. (17) who used them to anticipate significant blood loss and implement early blood-conserving strategies, establishing the Predictive Model of Transfusion in Spine Surgery (PMTSS). Four pre-operative risk factors were found to be independent predictors of transfusion; these included: an age greater than 50 years, a pre-operative haemoglobin (Hb) concentration less than 12 g/dL, fusion of more than two levels and surgeries requiring transpedicular osteotomies (17). The PMTSS was determined to be a reliable predictor of allogeneic transfusion, and therefore can be used to employ early blood-saving strategies (17). However, it should be noted that this model only included adult spine surgery patients and as such cannot be used in paediatric populations (where scoliosis surgery is more frequently performed).

During 2016, Pauyo et al. (8) developed the Canadian Consensus for the Prevention of Blood Loss in Spine Surgery. This cross-sectional study was conducted with 25 Canadian spine surgeons, where their experience was used to generate a consensus surrounding risk factors and preventative methods for significant blood loss in major spine surgery. The definition of significant blood loss was defined to be a blood loss of more than 25% of the patient’s total blood volume, based on the opinion of the spine surgeons (8). The risk factor that was found to have one of the most profound influences on blood loss was a prolonged operative time of greater than five hours; whilst appropriate intra-operative haemostasis was found to be the measure most effective in preventing blood loss (8). It was recommended by Pauyo et al. (8) that these factors be further evaluated in future large-scale studies to predict their effect on morbidity and mortality following spine surgery.

1.2.3 Transfusion Thresholds

An important aspect relating to available recommendations for blood transfusion in spine surgery is the lack of consensus surrounding appropriate thresholds for blood transfusions (8). Carson et al. (18) described in a review that using restrictive transfusion guidelines (Hb concentrations 7-8 g/dL) decreased patients exposed to transfusions by 43%; with no associated increases in morbidity or mortality. However, this review was not limited to spine patients and included a spectrum of clinical specialities.

Dick et al. (5) reported similar findings where lower transfusion thresholds were found to significantly decrease the risk of blood transfusion with no evidence of increased adverse outcomes. Similarly, restrictive transfusion triggers were also instituted by Ohrt-Nissen et al. (19), in their retrospective review of blood transfusions in operative management of idiopathic scoliosis. They reported use of a standardised national guideline, where a Hb of less than 7 g/dL was used to avoid unwarranted transfusions (19). However, these studies did not assess lower transfusion triggers in isolation, but rather in association with other transfusion reducing interventions.

A comparative analysis between the available literature is difficult as these studies frequently employ different blood conservation strategies in varying combinations (6). The data are also often presented in diverse forms and formats which further makes comparisons difficult (6). Hence, it is difficult to assess the efficacy of lower transfusion thresholds, as reported by Dick et al. (5) and Ohrt-Nissen et al. (19), in isolation as other transfusion reducing interventions may have contributed equally well to reducing the need for transfusion. Thus, greater attention and research needs to be directed to this topic.

Whilst use of restrictive Hb transfusion triggers is often quoted in literature, the amount of blood lost, and clinical features of the patient also need to be considered. The physiological response to blood loss and subsequent need for transfusion are related to the volume of blood loss (20). This can be categorised into patients with losses of <15%, 15-30%, 30-40% and >40%; where patients with blood loss of >30% have moderate to severe often requiring blood transfusion (20).

1.2.4 Estimation of Intra-operative Blood Losses

There is a large quantity of data and literature available on blood loss in spine surgery as it is a frequent concern for spine surgeons. However, a considerable limitation that must be recognised when blood losses are reported in the literature regards the accuracy of the intra-operative blood losses. These losses are reported as estimated blood loss (EBL) (21). Unfortunately, EBL is neither an easily reproducible nor strictly precise method of documenting blood loss. Nevertheless, it remains the only practical approach to documenting blood losses in theatre.

Shapiro and Sethna (21) in their systematic review of blood loss in paediatric spine surgery noted that there were differing ways of presenting blood losses in various papers. In some studies, EBL is quantified in either millilitres (mL) or cubic centimetres (cc), whereas other authors calculated blood loss as a percentage of estimated blood volume (EBV), where EBV is determined to be 70 mL/kg (21). Furthermore, Shapiro and Sethna (21) described the use of blood loss as a percentage of EBV to be of greater value in presenting blood loss as the patients' relative size, and therefore weight was taken into consideration.

1.2.5 Multifactorial Blood Management Strategy

As established, scoliosis surgery is associated with significant blood losses which leads to anaemia, hypotension, coagulopathy, and eventually a need for an allogeneic blood transfusion. Unfortunately, blood transfusions used to manage this are not without risk/cost (7, 14). This necessitates that the managing surgeon have additional measures available to decrease intra-operative blood loss and the need for a transfusion (4). For this reason, multiple interventions are often instituted simultaneously to decrease blood loss and reduce the need for allogeneic blood transfusion using a multidisciplinary blood management protocol. These interventions are separated into those for the pre-operative and intra-operative periods (5). Pre-operative interventions include stopping medications affecting blood coagulation and Hb optimisation (4, 5). Intra-operative measures include using antifibrinolytics, cell salvage, appropriate patient positioning, hypotensive anaesthesia, and the use of electrocautery (4).

Dick et al. (5), in a large retrospective cohort review, analysing 1039 procedures for children undergoing scoliosis correction surgery, reported a significant decline in allogeneic blood transfusions with the institution of multiple blood saving interventions. Transfusion rates amongst patients undergoing scoliosis surgery were found to be as high as 90% before the implementation of blood conserving interventions. However, once implemented the transfusion rates decreased to approximately 20% (5). Similarly, Hassan et al. (6) reported that the institution of a blood management protocol resulted in low transfusion rates. Unfortunately, these studies each used different approaches to managing blood loss and are therefore difficult to compare. Nonetheless, it is important to note that a multimodal approach to saving blood seems far more efficacious than the application of an isolated intervention. Therefore, in the proposed research study a multimodal approach to decreasing blood loss and allogeneic transfusions will be assessed and instituted.

1.2.6 Preoperative Interventions

The role and importance of pre-operative interventions implemented to reduce blood loss during the intra-operative period has gained greater prominence in recent literature. Pre-operative Hb optimisation includes screening for anaemia and bleeding disorders and providing supplemental haematinics (6). Hb optimisation, usually used in combination with other blood saving interventions, was found to be effective to ensure a target Hb concentration before spine surgery to decrease the risk of transfusion (5, 6). Dick et al. (5), reported institution of a Hb optimisation clinic where a pre-operative Hb of 12.5 g/dL was targeted, this value was chosen based on a review by Pinder et al. (22) which demonstrated that Hb less than 12.5 g/dL was associated with a need for transfusion.

Autologous blood transfusions are also mentioned as part of the pre-operative measures, unfortunately there is mixed evidence to support its use. The literature has even demonstrated a reciprocal increase in transfusion requirements with no differences in outcomes (23). Additionally, autologous blood transfusions do not completely mitigate the risk of allogeneic blood transfusions; with 40% of patients still requiring additional allogeneic transfusion (24). Therefore, this modality has fallen out of favour over the past two decades (4).

Another constituent of pre-operative intervention is the stopping of certain medications. These include non-steroidal anti-inflammatory drugs, antiplatelet agents, and anticoagulants (4). Each of these may directly or indirectly affect blood coagulation and hence increase the risk of peri-operative bleeding. Burger et al. (25) reported that in non-cardiac surgeries, the continued use of these medications increased the risk of bleeding complications by up to 1.5 times.

Pauyo et al. (8) further showed that spine surgeons preferred the discontinuation of antiplatelet agents as they believed this was a particularly important factor in limiting blood loss. Despite these findings, the preponderance of evidence has failed to prove any significant effect on blood loss in spine surgery. Therefore, there are currently only weak recommendations for stopping these medications prior to spine surgery (4). It should be noted that there is a paucity of studies specifically addressing medications affecting haemostasis in spine surgery, and subsequently this shows a need for further research focusing on this topic (8).

1.2.7 Antifibrinolytics

While various intra-operative blood loss prevention and management strategies are frequently used, the focus of many recent studies has been the use of antifibrinolytics and intra-operative cell salvage. Mikhail et al. (4) described antifibrinolytics as “one of the greatest advancements” in reducing blood loss in spine surgery. The use of these agents has been shown to decrease transfusion requirements by up to approximately 50% in those undergoing major surgery (26). The literature describes two agents that are frequently used: e-aminocaproic acid and tranexamic acid (TXA) (4).

TXA is a lysine analogue that decreases the breakdown of the fibrin clot by preventing the conversion of plasminogen to plasmin (27). In South Africa, TXA is the preferred antifibrinolytic drug used as it is more cost effective and offered in a generic form (4). In addition to this, TXA has been found to provide a greater haemostatic benefit. The dose of TXA frequently described was a loading dose of 10mg/kg and a maintenance dose of 1 or 2mg/kg/h (4). The utilisation of higher doses of TXA has been investigated in the literature, with loading doses as high as 50mg/kg and maintenance doses of 5mg/kg/h being described (4). Whilst complication rates with these higher doses were similar to conventional doses, there remains a paucity of level 1 evidence for the use of these higher doses and as such, the institution of higher doses is not recommended at present (4).

Sethna et al. (28), in their randomised control trial (RCT), reported a significantly decreased blood loss in patients with the use of TXA, with the EBL being approximately 1230 (+/- 535) mL for the antifibrinolytic group and 2085 (+/- 1188) mL in the control group ($p<0.01$). These findings were further supported by studies conducted by Lykissas et al. (29) and Goobie et al. (30), who similarly found a decreased loss with use TXA. A meta-analysis by Shrestha et al. (31) found that the average blood loss for patients receiving antifibrinolytics was 525.15 mL lower ($p<0.001$) and decreased the units of RBCs transfused. The use of TXA is supported by a high level of evidence and as such should be given in all patients going for surgery where blood loss is predicted (4).

1.2.8 Intra-operative Cell Salvage

Intra-operative cell salvage (ICS) is another available modality used for minimising the effect of blood loss. In it, blood from the operative field is drained and filtered to form an RBC concentrate that may then be transfused back into the patient (4). Its use has also been demonstrated to decrease the need for allogeneic blood transfusion (4-6, 32). In support of this, a retrospective case-control study by Bowen et al. (33), established that allogeneic blood transfusion rates were lower in the ICS group compared to patients who did not receive use of ICS i.e. 6% versus 55% ($p<0.05$).

Despite this, there remains a limitation that a minimum volume of blood loss is required to produce a unit for transfusion (4). Guidelines from the Association of Anaesthetists recommend ICS be considered in any procedure where blood loss is expected to be greater than 500ml or greater than 10% of total blood volume, and in cases where a tourniquet cannot be used (34). In patients undergoing scoliosis surgery (where large blood loss is predicted) ICS was only found to be cost neutral compared to allogeneic blood transfusion (35). In context of the South African setting, use of ICS may be an option to reduce allogeneic blood transfusion. Its availability and costs associated with setup and maintenance make its accessibility difficult. Nevertheless, this modality of managing intra-operative blood loss should be used if available for spine surgery.

1.2.9 Surgical Approach

Scoliosis surgery is performed by either a posterior, anterior or a combined (anterior and posterior) approach (5). The greatest blood loss is noted with the use of the combined approach, with a ten times greater chance of having to receive a transfusion (5). However, when comparing anterior and posterior approaches, the available literature indicates that posterior procedures cause more blood loss than anterior approaches. This can be explained due to the posterior approaches requiring extensive surgical exposure of highly vascular structures such as paraspinal muscles and vertebral elements (6). In addition to this, a larger number of vertebral levels are frequently fused by the posterior approach, as such predisposing to greater blood loss (21, 31).

It should be stated that posterior procedures are becoming more frequently performed in scoliosis surgery especially since the introduction of third generation instrumentation (36). Furthermore, the posterior approach is favoured as even severe scoliosis may be corrected because instrumentation with pedicle screws provides strong correction forces and purchase (36). Also, by foregoing the anterior approach, the risk of post-operative pulmonary compromise is avoided (36). Therefore, the surgical approaches used in a study should be thoroughly documented as the surgical approach influences blood loss.

1.2.10 Bone Scalpel

Use of the ultrasonic bone scalpel (UBS) has become increasingly popular and more widely used in numerous surgical specialities (14, 37). While the use of UBS is not new, recent enhancements in its design have allowed it to become more widely adopted (37). It can efficiently cut bone whilst sparing and preventing damage to soft tissues. Bone is cut by high-speed oscillation of the blade whereas the elastic nature of soft tissue absorbs the force of the UBS, minimising blood loss (9, 14, 37).

Bartley et al. (37) demonstrated that use of UBS in the correction of idiopathic scoliosis resulted in significantly less blood loss when compared with standard osteotomy techniques ($p < 0.05$). EBL was reported to be 550 +/- 359 mL in patients who received UBS versus 799 +/- 383 mL in the control group. Importantly, surgical times were found to be comparable and there were dural tears in either group (37). Furthermore, Wahlquist et al. (14) in their retrospective cohort of 81 patients, supported that the use of UBS was effective in decreasing blood loss whilst not adversely modifying surgical time. While no level 1 evidence currently exists to validate these findings in idiopathic scoliosis, the available literature is promising regarding its usage.

1.3 Study Aim and Objectives

The aim of this study is to review intra-operative blood loss in patients who underwent posterior corrective surgery for idiopathic scoliosis at Chris Hani Baragwanath Academic Hospital (CHBAH).

Specific objectives include:

1. To measure overall intra-operative blood loss and the amount of allogeneic RBC used intra-operatively in scoliosis surgery.
2. To identify modifiable factors that may affect intra-operative blood loss including the use of TXA, ICS, UBS, and duration of surgery.
3. To establish recommendations and/or guidelines for reducing and possibly predicting intra-operative blood loss and allogeneic blood transfusion based on factors that were found to affect blood loss.

Chapter 2

Methodology

2.1 Research Question

What is the intra-operative blood loss and the modifiable intra-operative factors that influence blood loss in patients who undergo posterior corrective surgery for idiopathic scoliosis at CHBAH?

2.2 Research Design

This study was a retrospective record review of patients who underwent posterior corrective surgery for the treatment of idiopathic scoliosis in the Spine Unit within the Department of Orthopaedic Surgery at CHBAH

2.3 Materials and Methods

Preceding any data collection, approval to conduct the study was attained from both the Human Research Ethics Committee (HREC)(Medical) of the University of the Witwatersrand (refer to Appendix A) and the Medical Advisory Committee (MAC) of CHBAH (refer to Appendix B). Furthermore, every patient included in the study was designated a study number to maintain anonymity and confidentiality.

Once patients who underwent corrective scoliosis surgery were identified, their files were retrieved from the patient records archive. Following this, patients assessed to be eligible for inclusion in the study were identified and their data were collected using a data collection sheet (refer to Appendix C).

2.4 Selection Criteria

All patients admitted at CHBAH who underwent posterior corrective surgery for idiopathic scoliosis during the period of 01 January 2015 to 31 December 2020 were chosen as part of the study sample. This was indiscriminate of age, gender, or severity of the deformity. Importantly, during this period the Spine Unit at CHBAH moved to managing idiopathic scoliosis as a single stage posterior approach rather than a staged combined anterior and posterior approach. The identification of these patients was done by examining the orthopaedic spine theatre register at CHBAH with selection based on the following criteria:

Inclusion criteria

1. All patients who underwent posterior corrective scoliosis surgery.

Exclusion criteria

1. Patients with scoliosis secondary to an identifiable cause, such as:
   a. Congenital: hemivertebra, failure of segmentation.
   b. Neuromuscular: cerebral palsy, spinal muscular atrophy.
   c. Syndromic: Connective tissue disorders including Ehlers-Danlos syndrome and Marfan syndrome.
   d. Degenerative scoliosis.
2. Patients requiring revision of previous scoliosis surgery.
3. Lost or inadequate hospital records - poor documentation relating to surgery, blood loss and transfusion.

2.5 Data Collection

All study data were collected by the study investigator (Dr M.H.S. Aftab). Initially, as noted above, patients who underwent posterior corrective scoliosis surgery were identified by using the orthopaedic spine theatre register at CHBAH. This method identified a total of 49 patients who had undergone corrective scoliosis surgery between 2015 and 2020. From these, 6 patients were excluded as they received corrective surgery for secondary scoliosis or revision surgery. Following this, records of the remaining 43 patients were attempted to be retrieved from the patient record archive at CHBAH. A further 7 patients were excluded as 3 patients lacked adequate hospital records (critical data relating to the patient or surgery was missing) while 4 had files that were either lost or could not be traced.

A thorough review of the files was undertaken on the remaining 36 patients, who all met the necessary prerequisites for inclusion in the study. The data collection sheet (refer to Appendix C) was then used to collect this information. Basic demographic data including the age and gender were collected. Furthermore, weight, pre-operative Hb, idiopathic scoliosis Lenke type and magnitude of the main curve (expressed as the cobb angle) were documented. Details regarding the surgery were also noted including EBL, the duration of the surgery, the number of segments fused, use of TXA, ICS and UBS, and if transfusion of allogeneic RBC was needed, including the number of units transfused. EBL was approximated by the anaesthetic team based on the number of swabs used intra-operatively with each full swab being 100mL of EBL (38), and the blood volume collected via suction or ICS using a visual estimation method.

Additionally, the EBV of each individual patient was determined using the formula: Body weight (kg) x 70 mL=EBV (in mL). This was used to further quantify EBL as a percentage of EBV to better account for blood loss based on patient weight. Finally, the post-operative Hb was also noted, the day following surgery. Following collection of this information, it was subsequently captured and stored on a Microsoft Excel spreadsheet (Excel for Microsoft 365, version 2202, build 16) for further data analysis.

2.6 Data Analysis

The data were analysed using the Stata version 17.0 statistical software package (Stata Corp, Collage Station, TX). At this point, data cleaning and analysis was done using the Stata software suite. Descriptive statistics were used to analyse the socio-demographic profile of the participants, blood loss parameters and blood transfusion parameters, these were reported as frequency and percentages for categorical variables and are described further in the results chapter. The mean and standard deviation (SD) were reported for continuous variables which had a normal distribution, whilst non-normal distributed data were described using the median and interquartile range (IQR).

Inferential statistics were used to further delineate the relationship between the variables. For this, linear regression analysis was used to assess the relationship between EBL, EBL as a percentage of EBV and the volume of blood transfused. Additionally, the independent Student's t-test was used to determine if there was a difference in the mean EBL in patients who received TXA *versus* patients who did not receive TXA. Similarly, this was also applied to intra-operative use of ICS and UBS. The dependent Student's t-test was also used to compare the patients' pre- and post-op Hb levels. Linear regression was again used to establish the relationship between EBL and duration of surgery, number of segments fused, Lenke type and

Cobb angle. P - values < 0.05 were considered statistically significant. Final data analysis was done on a total of 36 participants.

Chapter 3

Results

3.1 Socio-demographics Factors

A total of 36 patients met the inclusion criteria for the study. Of these, female patients constituted the majority; with the study including 30 females (83.33%) and 6 males (16.67%), as demonstrated in Figure 3.1. Furthermore, patients included in the study had ages ranging from 11 to 30 years old. The median age of the patients was 16 (IQR: 13-17) years with most of them being less than 20 years old, as 33 (91.67%) were younger than 20 years old while only 3 (8.33%) were either 20 years of age or older. The mean weight of patients was 46.31(+/- 3.52) kg ranging from a minimum of 34 kg to a maximum of 60 kg. The data are presented in Table 3.1 below.

Table 3.1: Socio-demographic information

Characteristic	Mean (SD)	Frequency (%)
Age		
< 20 years old	-	33 (91.67%)
> 20 years old	-	3 (8.33%)
Gender		
Female	-	30 (83.33%)
Male	-	6 (16.67%)
Weight	46.31 (+/- 6.67) kg	-

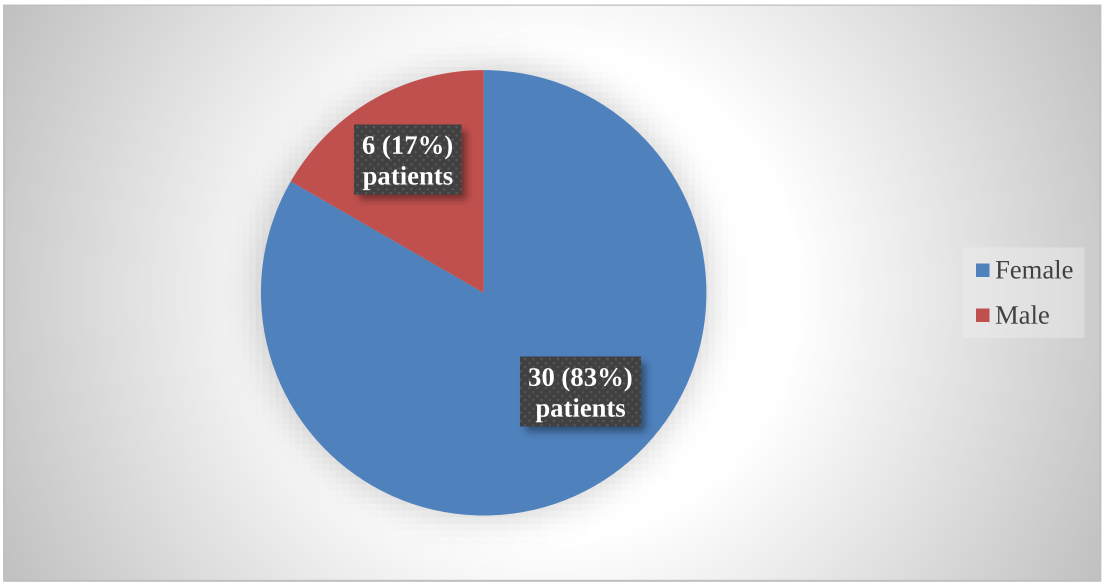

Figure 3.1: Gender distribution of the study population

3.2 Surgeries Performed Each Year

A further audit of the number of surgeries done each year was completed. The median number of surgeries performed was 5.5 (IQR: 5-7). It was found that 10 (27.78%) patients had surgery in 2015, 5 (13.89%) patients in 2016, 7 (19.44%) patients in 2017, 5 (13.89%) patients in 2018, 6 (16.67%) patients in 2019 and 3 (8.33%) patients in 2020 (refer to Figure 3.2). Therefore, the greatest number of surgeries were done in 2015, whilst the least number of surgeries were done in 2020.

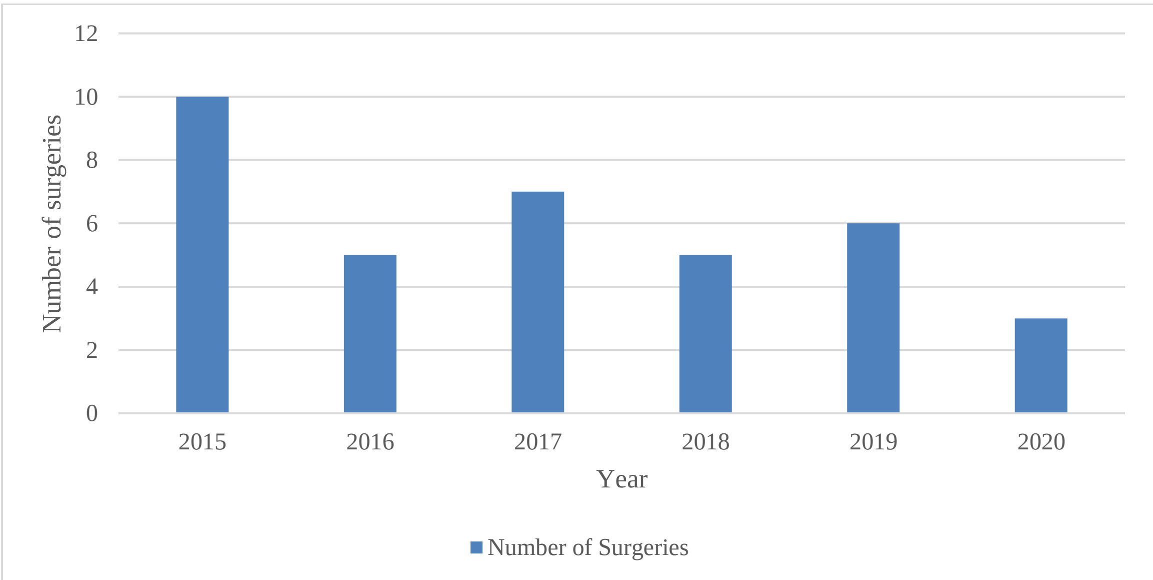

Figure 3.2: Number of surgeries performed per year

3.3 Pre- and Post-operative Hb

When assessing blood loss, the mean pre-operative Hb was 13.76 (+/- 1.9) g/dL, with the lowest pre-operative Hb being 11.1 g/dL and the highest being 16.6 g/dL; whereas the mean post-operative Hb was 10.85 (+/- 1.39) g/dL with lowest post-operative Hb being 8.2 g/dL and the highest being 15.1 g/dL (refer to Table 3.2). Furthermore, there were only 4 (11.11%) patients that had a pre-operative Hb of less than 12.5 g/dL, and of these 2 patients required blood transfusion.

When comparing pre- and post-operative Hb, the mean difference was determined to be 2.91 g/dL and was statistically significant (p=0.036). As such, the mean pre-operative Hb was greater than the post-operative Hb, thus demonstrating a significant decline in Hb following surgery.

Table 3.2: Comparison of pre- and post-operative Hb

	Mean (SD)	**95% Confidence Interval**
Pre-operative Hb	13.76 (+/- 1.9) g/dL	13.2 - 14.1 g/dL
Post-operative Hb	10.85 (+/- 1.39) g/dL	10.3 - 11.3 g/dL
Difference	2.91 g/dL	2.2 - 3.4 g/dL

3.4 Blood Loss During Surgery

The mean EBL was 722.22 (+/- 328.30) mL, with it ranging from 300 mL to as high as 1600 mL (refer to Table 3.3). The average EBV, calculated using the equation presented in section 2.6, was 3241.58 mL with results varying from 2380 mL to 4200 mL.

When analysing the blood loss as a percentage of EBV, the results showed a mean blood loss of 22.99 (+/- 11.61) % with a range from as low as 6.49% to as high as 50.79% (refer to Table 3.3). Furthermore, EBL as a percentage of EBV was further divided into patients who had a blood loss of <15%, 15-30%, 30-40% and >40%. Of these, 7 (19.44%) patients had a blood loss of <15%, 17 (47.22%) patients had a blood loss between 15-30%, 9 (25%) patients had a 30-40% blood loss and lastly 3 (8.33%) patients had a blood loss of >40% (refer to Figure 3.3).

The majority of the patients had a blood loss between 15-30%. Blood losses >30% only ever occurred in the first three years (i.e. between 2015-2017) whereas the greatest number of patients that had a blood loss of <15% was in 2019.

Table 3.3: Blood loss during surgery

	Mean (SD)	**95% Confidence Interval**
EBL	722.22 (+/- 328.30) mL	611.13 - 833.30 mL
EBL as a percentage of EBV	22.99 (+/- 11.61) %	19.06 - 26.92 %

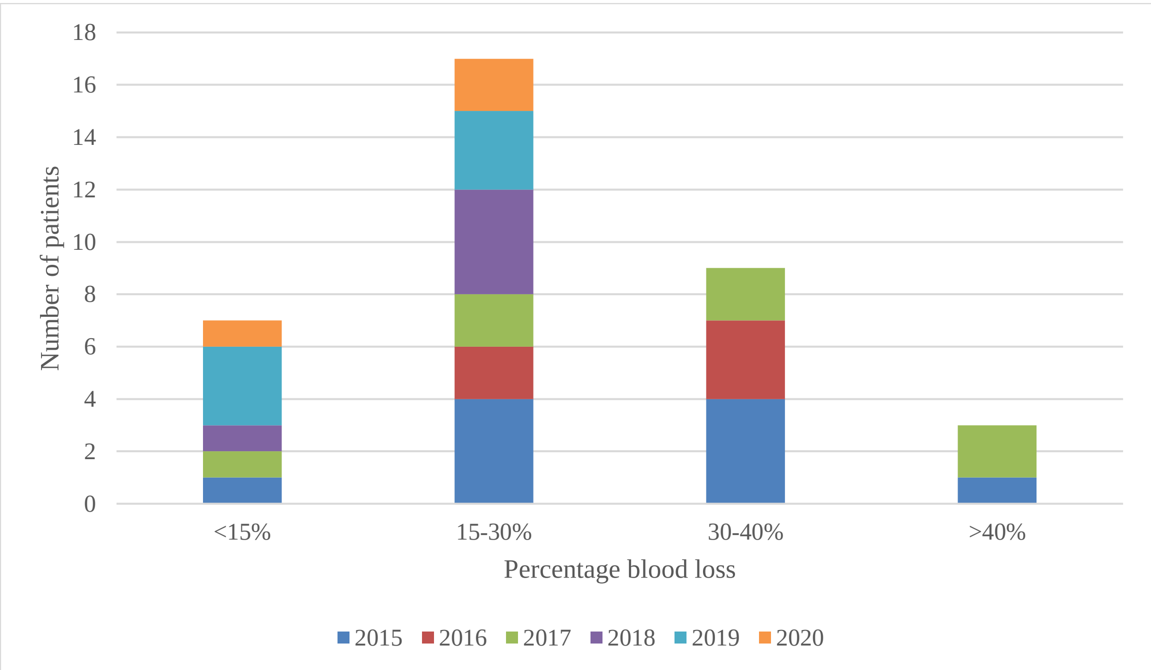

Figure 3.3: Distribution of percentage EBL per year

3.5 Blood Transfusion During Surgery

During surgery, a total of 11 (30.56%) patients received a blood transfusion whereas the remaining 25 (69.44%) patients did not require a transfusion (refer to Figure 3.4). Of the patients who received a blood transfusion, 4 (36.36%) received 1 unit, a further 4 (36.36%) patients received 2 units, 2 (18.18%) patients received 3 units and finally 1 (9.1%) patient required 4 units of RBC concentrate for transfusion (refer to Figure 3.5).

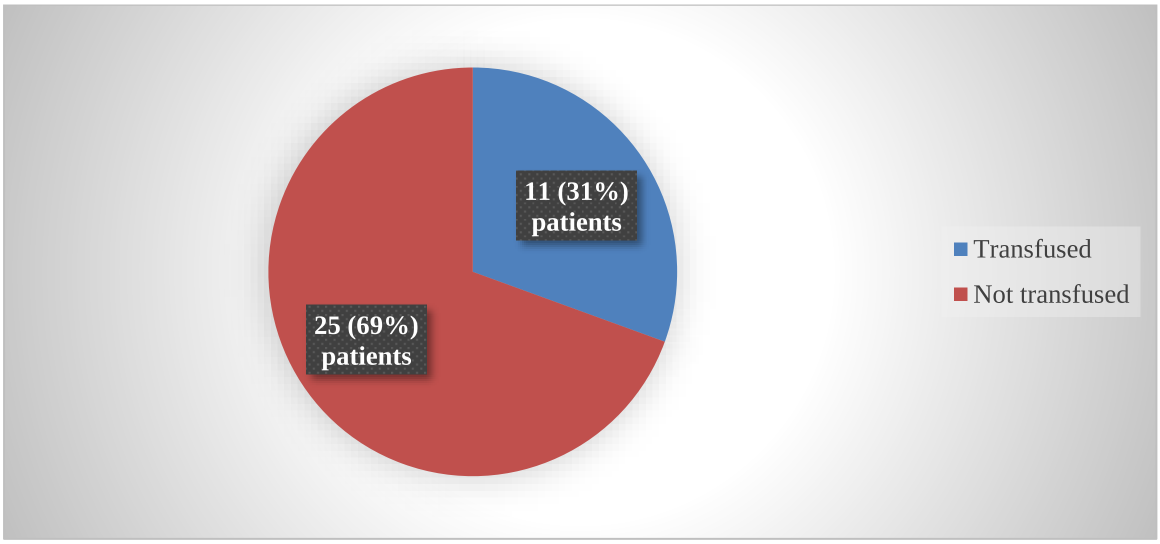

Figure 3.4: Comparison of the number of patients transfused or not transfused

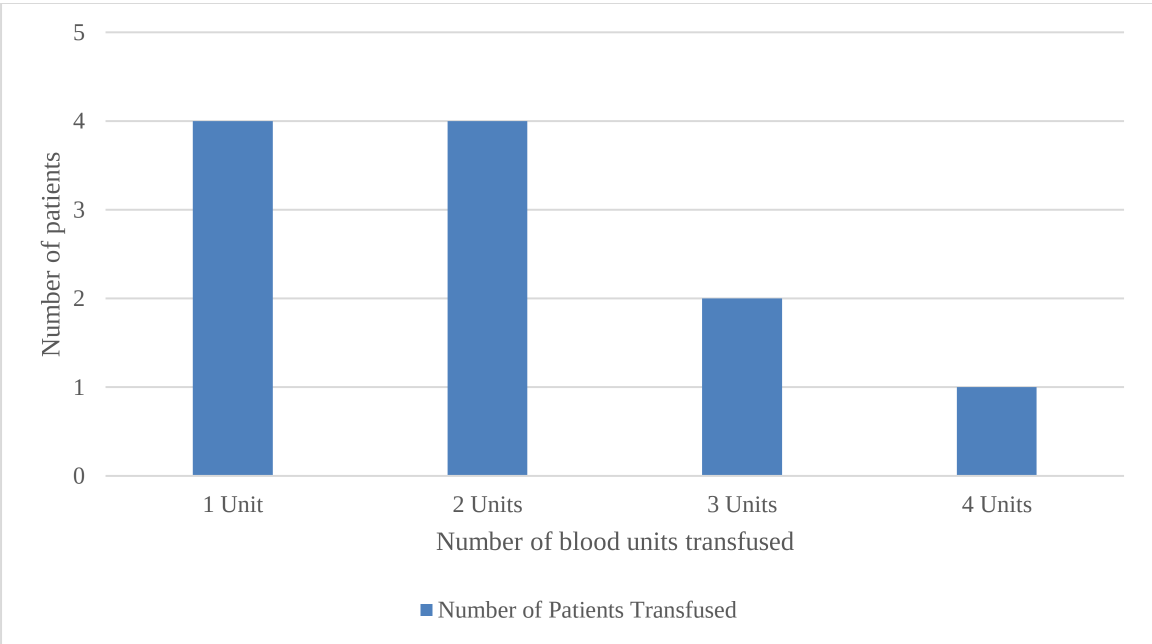

Figure 3.5: Number of units of blood received amongst patients transfused

Of the 11 patients who received a transfusion, 9 (81.82%) patients were transfused between 2015-2017; whereas 2 (18.18%) patients received a transfusion between 2018-2020. Additionally, only 1 of the 2 patients who were transfused in the last three years required a transfusion of more than 3 units (refer to Figure 3.6).

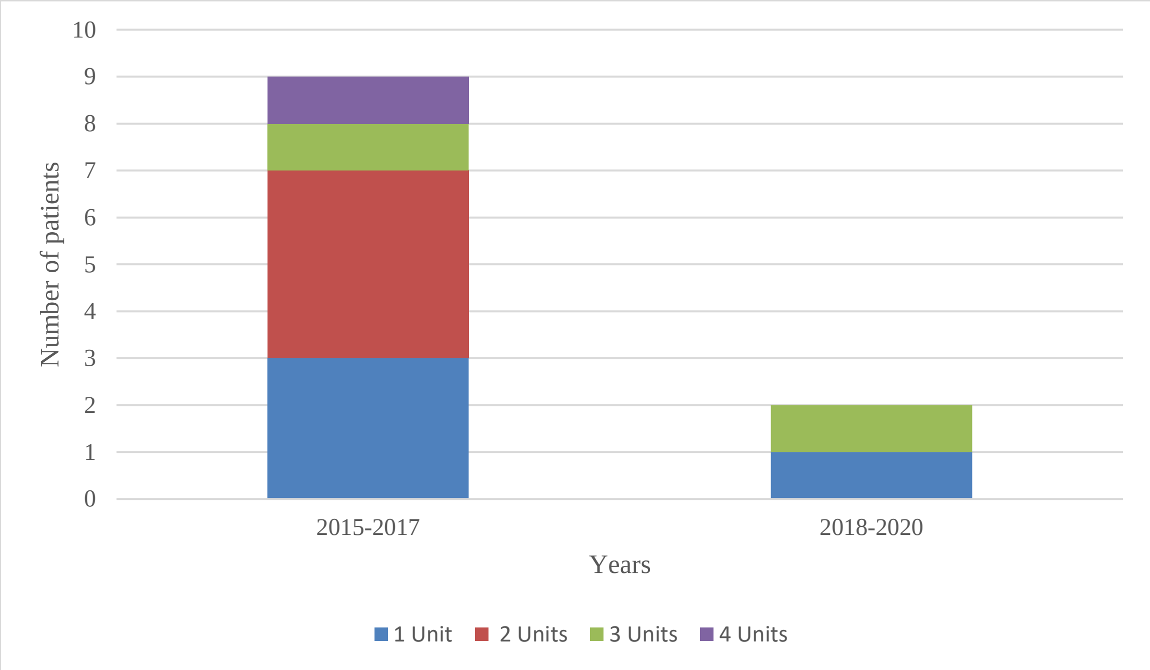

Figure 3.6: Comparison of number of units transfused in the first and last three years of study

Univariate linear regression showed a statistically significant association between EBL and the volume of blood transfused (p=0.005) i.e. for every 139.58 mL of blood lost, 1 unit of blood was transfused (refer to Table 3.4). Additionally, when assessing this association in terms of EBL as a percentage of EBV in patients that were transfused, it was found that a blood loss of 5.82% correlated with a transfusion of 1 unit of blood. This was also found to be statistically significant (p=0.001).

Table 3.4: Correlation between blood loss parameters and blood transfused

	Coefficient	95% Confidence Interval	p-value
EBL	139.58	45.08 - 234.10	0.005
EBL as a percentage of EBV	5.82	2.65 - 8.98	0.001

3.6 Intra-operative use of TXA

Twenty-one (58.33%) patients received TXA while 15 (41.67%) patients did not receive TXA. It is important to highlight that all the patients operated on from May 2017 onwards received TXA, which constituted a total of 19 (90.48%) patients and 52.78% of the total patients; whereas before this period, only 2 patients received TXA (refer to Figure 3.7).

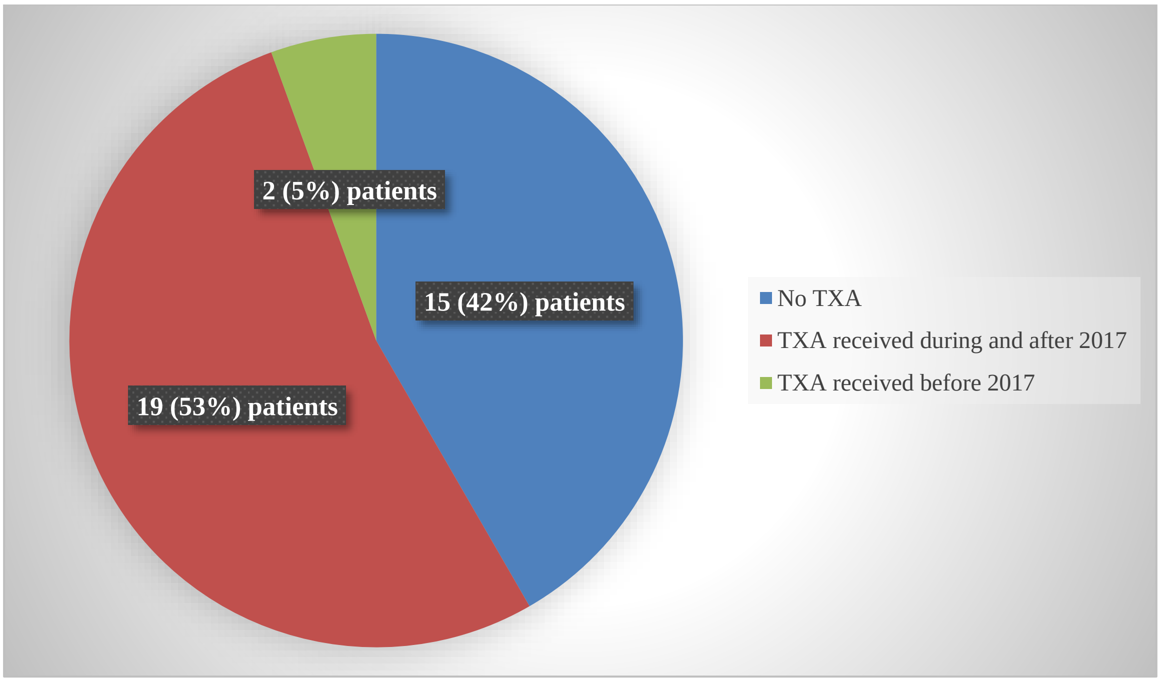

Figure 3.7: Comparison of intra-operative usage of TXA

Moreover, an analysis comparing patients who received TXA versus those who did not was subsequently done (as shown in Table 3.5). It was determined that patients who received TXA had a lower mean EBL of 602.38 (+/- 219.93) mL compared to patients who did not receive TXA with a mean EBL of 890 (+/- 385.54) mL. The mean difference of 287.62 mL was statistically significant (p=0.018).

Table 3.5: Comparison of blood loss in patients given and patients not given TXA

	Mean (SD)	95% Confidence Interval	p-value
Received TXA	602.38 (+/- 219.93) mL	502.27 - 702.49 mL	0.018
No TXA	890 (+/- 385.54) mL	676.49 - 1103.51 mL	
Difference	287.62 mL	81.90 - 493.33 mL	

3.7 Intra-operative use of ICS

During the duration of the study, only 3 (8.33%) patients received the use of ICS whereas 33 (91.67%) patients did not. The average ICS volume measured was 739.37 mL. The EBL in patients who received ICS was 1033.33 (+/- 152.75) mL and the EBL in patients who did not receive ICS was 693.93 (+/- 326.38) mL (refer to Table 3.6). When compared, it was found that patients who received ICS lost 339.39 mL more blood than patients who did not receive ICS however, this was not statistically significant (p=0.194). Additionally, all patients who received ICS had blood losses of >30% of EBV.

Table 3.6: Comparison of blood loss in patients given and patients not given ICS

	Mean (SD)	95% Confidence Interval	p-value
ICS done	1033.33 (+/- 152.75) mL	653.88 - 1412.79 mL	0.194
No ICS	693.93 (+/- 326.38) mL	578.21 - 809.67 mL	
Difference	-339.39 mL	-730.08 - 51.29 mL	

3.8 Intra-operative use of UBS

Similarly, to the use of TXA, the first documented use of UBS was in August 2017, after which all cases received intra-operative use of UBS. As such, 18 (50%) patients had intra-operative use of UBS while the remaining 18 patients did not. Additionally, when comparing the EBL in patients who received intra-operative use of UBS versus those who did not, the data indicated that patients in whom UBS was used had a lower mean blood loss i.e., 558.33 (+/- 199.45) mL when UBS was utilised versus 886.11 (+/- 353.89) mL when UBS was not utilised (refer to Table 3.7). The mean difference of 327.78 mL was found to be statistically significant (p=0.01).

Table 3.7: Comparison of blood loss with and without the use of UBS

	Mean (SD)	95% Confidence Interval	p-value
UBS Used	558.33 (+/- 199.45) mL	459.15 - 657.52 mL	0.01
No UBS	886.11 (+/- 353.89) mL	710.13 - 1062.10 mL	
Difference	327.78 mL	133.20 -522.36 mL	

3.9 Additional Factors Contributing to Blood Loss

The average duration of each surgery was approximately 355 (+/- 75.38) minutes, with the duration ranging from a minimum time of 180 minutes to a maximum time of 525 minutes. Furthermore, univariate linear regression showed an association between EBL and the duration of surgery, as every minute spent in theatre during surgery resulted in 1.63 mL of blood loss (p=0.025) (refer to Table 3.7).

The average number of segments fused was 10.25 (+/- 1.87) segments per surgery. As demonstrated in Figure 3.8, most patients received fusion of between 10 and 11 segments, which constituted 15 (41.67%) patients. It was determined that the number of segments fused also influenced the EBL, as every segment fused during surgery resulted in 80.24 mL of blood loss. This relationship was found to be statistically significant (p=0.005) (refer to Table 3.8).

Other parameters were tested for significance but did not show any statistically significant correlation with blood loss. These factors included the scoliosis Lenke type and the Cobb angle. With regards to the Lenke type, 13 (36.11%) patients were type 1, 4 (11.11%) patients were type 2, 14 (38.89%) were type 3, 1 (2.78%) patient was type 4, 3 (8.33%) were type 5 and 1 (2.78%) patient was type 6. As such, the two commonest types (type 1 and 3) constituted 27 (75%) patients. Furthermore, the median cobb angle of the study population was 60 (IQR: 52.5-80) degrees.

Table 3.8: Correlation of factors influencing EBL

Factor influencing blood loss	Coefficient	95% Confidence Interval	p-value
Duration of surgery	1.63	0.22 - 3.03	0.025
Segments fused	80.24	25.92 - 134.57	0.005
Lenke type	-45.68	-126.90 - 35.54	0.261
Cobb angle	1.65	-5.17 - 8.49	0.625

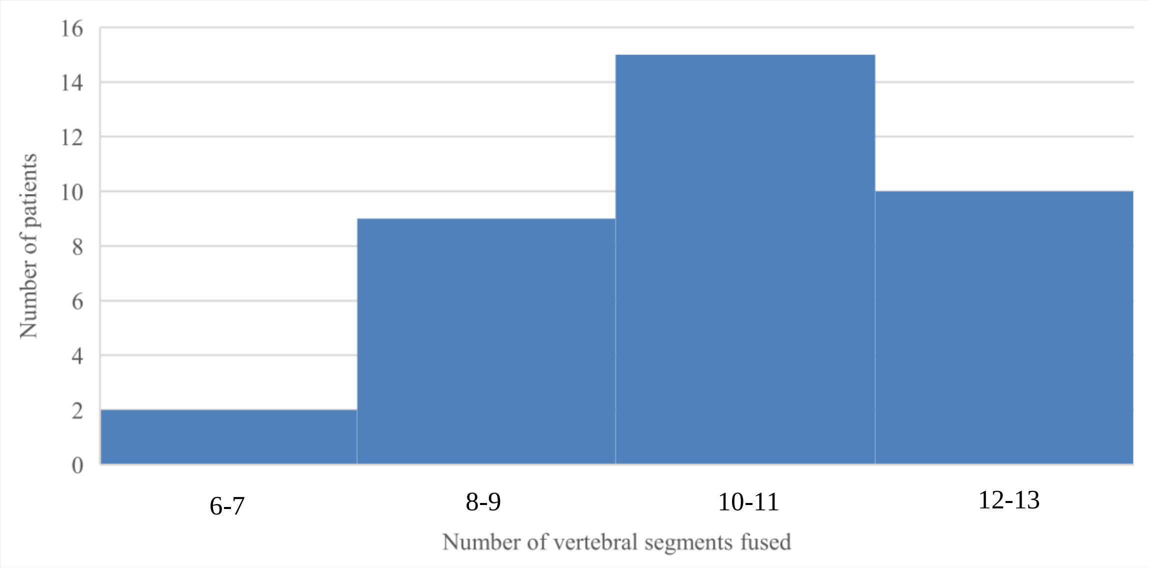

Figure 3.8: Comparison of the number of vertebral segments fused

3.10 Multivariate Analysis of Factors Contributing to Blood Loss

Multivariate linear regression was used to determine whether factors found to be univariately statistically significant correlated with EBL. These factors included the use of TXA and UBS, duration of surgery and the number of segments fused. The analysis showed no statistically significant correlations between the above-mentioned factors and EBL ($p>0.05$) (refer to Table 3.9).

Table 3.9: Multivariate analysis of factors contributing to blood loss

	Coefficient	95% Confidence Interval	p-value
Use of TXA	-193.06	-533.76 - 147.64	0.256
Use of UBS	-78.64	-430.20 - 272.92	0.651
Duration of surgery	1.24	-0.06 - 2.54	0.062
Segments fused	31.29	-25.97 - 88.56	0.273

Chapter 4

Discussion

4.1 Socio-demographics Factors

Adolescent idiopathic scoliosis (AIS) has frequently been associated and known to have a preponderance for the female gender (1, 2). Similarly, patients in the present study were primarily female, constituting 30 (83.33%) patients in the study cohort. This finding was consistent with results reported in similar studies regarding blood loss in the surgical management of idiopathic scoliosis. Chiu et al. (15) in their prospective review of blood loss during posterior spinal instrumentation for idiopathic scoliosis demonstrated similar demographics where 89% of patients enrolled in their study were female. Correspondingly, retrospective record reviews also demonstrated a female predominance ranging from 67.9% found by Dick et al. (5) to 84.29% shown by Ohrt-Nissen et al. (19) in their respective studies. This tendency towards the female gender has been postulated to be linked to X-linked dominant inheritance, however this continues to be an area of ongoing investigation (2).

The median age in the current study's population was 16 (IQR: 13-17) years, with 33 (91.67%) patients being younger than 20 years old. These findings cohere with the available literature. Dick et al. (5) reported a median age of 14 (IQR: 13-16) years in patients who underwent surgery. Ohrt-Nissen et al. (19) reported a mean age of 16.2+/-2.5 years whereas Chiu et al. (15) reported a mean age of 17+/-5.8 years. The youngest patient in the current study cohort was 11 years old and therefore, all the patients met the criteria to be classified as AIS.

Interestingly, 3 (8.33%) patients in this study were 20 years of age or older. Often, patients with idiopathic scoliosis requiring surgery are identified early and taken for posterior instrumentation to prevent deformity progression (1). Unfortunately, within the South African setting, systemic problems very often lead to delays in surgery. Some of these delays include the large number of patients who require surgery with limited theatre time, few specialist spine surgeons to attend to these patients and poor health seeking behaviour of patients that leads to a delay in seeking help at an appropriately early stage. All these factors lead to delays in surgery and could explain why the patient population included some older patients.

4.2 Surgeries Performed Each Year

In the present study, a review of the number of surgeries performed each year was undertaken. The median number of surgeries completed between 2015- 2020 was 5.5 (IQR: 5-7). Additionally, the number of surgeries performed between 2016-2019 fell within this IQR. Most patients were done in 2015, where 10 (27.78%) patients received surgery; whilst 2020 represented 3 (8.33%) patients of the study cohort who underwent surgery. This represents the lowest number of surgeries performed in any given year of the present study. One of the biggest contributing factors to this was the coronavirus disease (COVID-19) pandemic. During this time, most outpatient departments were closed, and elective surgeries were halted, which resulted in fewer patients with idiopathic scoliosis being surgically treated. As a result of the COVID-19 pandemic, many cases that would have been done during this period were cancelled and moved to the following year

4.3 Pre- and Post-operative Hb

Patients were noted to have a mean pre-operative Hb of 13.76 (+/- 1.9) g/dL whilst the lowest pre-operative Hb was 11.1 g/dL. Moreover, 4 (11.11%) patients had a pre-operative Hb of less than 12.5 g/dL. Of these patients, half required a RBC transfusion. Few studies exist where the authors examined the relationship between preoperative Hb and RBC transfusion in surgery for idiopathic scoliosis. Whilst a preoperative Hb of less than 12.5 g/dL has been demonstrated to be associated with a need for blood transfusion, this relationship has not been evaluated in isolation but rather as part of a multi-disciplinary approach to reducing the need for a RBC transfusion (5, 22). Nevertheless, the use of this cut-off is prudent as it allows for the institution of routine preoperative monitoring in patients undergoing surgery for idiopathic scoliosis. The mean post-operative Hb was 10.85 (+/- 1.39) g/dL, whilst the lowest post-operative Hb was 8.2 g/dL. As such, all patients had a post-operative Hb of greater than 7 g/dL which is the cited cut-off for transfusion (18, 19). However, it is important to note that the clinical condition of the patient needs to also be considered when deciding whether to transfuse (18).

4.4 Blood Loss During Surgery

Patients with idiopathic scoliosis undergoing posterior instrumented correction are at an increased risk of experiencing substantial blood loss (15). This is related to the large incision, extensive soft tissue dissection and prolonged operative times (4-6, 15). The mean EBL of patients in this study was 722.22 (+/- 328.30) mL whilst the mean blood loss as a percentage of EBV was 22.99 (+/- 11.61) %. These values corresponded to other similar studies involving posterior correction of idiopathic scoliosis. Hassan et al. (6), in their retrospective cohort review of 110 patients, reported very similar values, with a blood loss of 833 (+/- 462) mL and an EBL as a percentage of EBV of 23 (+/- 13) %. Additionally, Chiu et al. (15) described a mean blood loss of 951.0 (+/- 454.0) mL with an EBL as a percentage of EBV of 32.1 (+/- 21.4) %. These data are presented in Table 4.1 below.

Table 4.1: Comparison of EBL and EBL as a percentage of EBV

Study	EBL (mL)	EBL as a percentage of EBV (%)
Present Study	722.22 (+/- 328.30)	22.99 (+/- 11.61)
Hassan et al. (6)	833 (+/- 462)	23 (+/- 13)
Chiu et al. (15)	951.0 (+/- 454.0)	32.1 (+/- 21.4)

In a systematic review by Shapiro and Sethna (21), the authors appraised multiple studies regarding idiopathic scoliosis. They determined the mean EBL of patients undergoing posterior correction ranged from 600 mL to 1000 mL in the reviewed literature, which was consistent with the findings reported in the current study. Additionally, different authors favoured different methods of comparing data regarding blood loss in surgery for idiopathic scoliosis. For instance, Ohrt-Nissen et al. (19) reported EBL by dividing it into two groups i.e. patients who received a RBC transfusion and those who did not. Moreover, the authors of many studies did not use EBL as a percentage of EBV.

In the present study, blood loss that was expressed as EBL as a percentage of EBV was further categorised based on the extent of blood loss, i.e. <15%, 15-30%, 30-40% and >40%. It was found that 17 (47.22%) patients had a blood loss between 15-30%, making it the commonest blood loss category. This could be accounted for by blood loss of <30% occurring every year in this study (2015-2020); whereas blood losses of >30% only ever occurred in the first three years (2015-2017). Therefore, blood loss <30% occurred over a longer time interval hence why the greatest number of patients fell into this category.

Furthermore, it should be noted that all patients from May 2017 onwards received TXA, whilst all patients from August 2017 onwards received the use of both TXA and UBS. The institution of these interventions into the management of idiopathic scoliosis had a potentially profound effect on the blood loss, as demonstrated by the sudden decline in patients with a blood loss >30% between 2018-2020. This possibly indicates the efficacy of these factors in reducing blood loss. In addition, it was found that the largest number of patients with a blood loss of <15% was in 2019. This finding again highlights the effectiveness of the factors previously implemented and could likely be explained by improved proficiency, understanding and implementation of the blood conserving strategies during the duration of the study.

4.5 Blood Transfusion During Surgery

Patients with idiopathic scoliosis undergoing corrective surgery remain a group at high risk of receiving a RBC transfusion due to the frequently large volumes of blood lost during the procedure (5-7, 19). This topic remains an area of interest as a significant cost and morbidity can be associated with use of allogeneic blood transfusion (4, 12). In this study, a total of 11 (30.56%) patients received a blood transfusion. These findings were similar to and concurred with those reported in the available literature. Ohrt-Nissen et al. (19) reported a transfusion rate of 30.48%; whilst Dick et al. (5) reported a transfusion rate of 24.4%. The lowest rate was noted by Hassan et al. (6) who found a transfusion rate of 14.15% (refer to Table 4.2).

Patients who received blood transfusions were further grouped according to the number of units of RBC transfused. It was ascertained that the commonest number of units transfused, in this study, included both one and two units of RBC. Both groups had the same number of patients i.e. 4 (36.36%) patients who received RBC transfusion. The remaining 3 (27.78%) patients received three or more units of RBC. Parallel to these findings, Ohrt-Nissen et al. (19) also documented and divided patients according to the number of units of RBC transfusions. They reported that 32% of patients received one unit of RBC, 38% of patients received two units and 30% of patients received three or more units of RBC (19).

Table 4.2: Comparison of the percentage of patients transfused

Study	Patients transfused (%)
Present study	30.56
Ohrt-Nissen et al. (19)	30.48
Dick et al. (5)	24.4
Hassan et al. (6)	14.15

Furthermore, 9 (81.82%) patients had transfusions between 2015-2017, whereas only 2 (18.18%) patients had transfusions between 2018-2020. Additionally, of the patients who received more than three units of blood transfusion, 2 (66.67%) patients had transfusions between 2015-2017. These results adhere to the previous findings of diminished blood losses which occurred between 2018-2020. The finding of diminished blood losses and RBC transfusions together during this period possibly highlight and reinforce the efficacy of the blood conserving measures implemented during this period. Similarly, Dick et al. (5) reviewed the rate of transfusion before and after the implementation of a multidisciplinary blood conservation program. They reported that the average number of patients transfused was 89.2% before versus 20.1% after the institution of the program. In addition, the mean number of units transfused decreased from as high as 9.1 units before program implementation to 2.1 units after its implementation (5).

Further analysis of EBL and RBC transfusions established a relationship using univariate linear regression. It was found that for every 139.58 mL of blood lost, this resulted in a one unit RBC transfusion (p=0.005). Similarly, a loss of every 5.82% of the total EBV resulted in a transfusion of one unit of RBC (p=0.001). These findings were consistent with previous results reported in this study, which demonstrated that higher rates of transfusions occurred with greater blood losses i.e. the largest blood losses and greatest rates of blood transfusions occurred concurrently between 2015-2017.

4.6 Intra-operative use of TXA

Use of antifibrinolytics, specifically TXA, in posterior corrective surgery for idiopathic scoliosis has recently gained added popularity as more literature continues to demonstrate its efficacy (27). In the current study, 21 (58.33%) patients received TXA while 15 (41.67%) patients did not. Intriguingly, of the patients who received TXA, only 2 (9.52%) patients received it before May 2017, whereas after this period, all patients undergoing corrective surgery received TXA. On reviewing the available literature for TXA usage in surgery for idiopathic scoliosis, it became apparent that most of the literature regarding its use gained prominence from 2017 onwards. Only seven studies had ever been published before 2017, whereas 15 new studies had been published after this time (39). Based on the growing body of evidence in favour of TXA usage during 2017, the Spine Unit at CHBAH decided the introduction of TXA into their surgical management of idiopathic scoliosis would be prudent.

To further evaluate the effect of TXA on blood loss, EBL was compared amongst patients who received TXA and patients who did not. It was found that patients who received TXA had a lower mean EBL of 602.38 (+/- 219.93) compared to the mean EBL of 890 (+/- 385.54) mL in patients who did not receive TXA. Additionally, the mean difference of 287.67 mL (p=0.018) demonstrated that the use of TXA had a statistically significant effect on reducing blood loss in posterior surgery for idiopathic scoliosis. This finding again reinforced the previous result of decreased blood losses between 2018-2020 establishing that the introduction of TXA certainly influenced the reduction of blood loss.

RCTs conducted by Sethna et al. (28), Lykissas et al. (29), and Goobie et al. (30) similarly demonstrated a reduced blood loss with the administration TXA (refer to Table 4.3). Likewise, Shrestha et al. (31) validated that TXA was not only effective in reducing blood loss during surgery for idiopathic scoliosis, but also at decreasing rates of transfusion. These findings by Shrestha et al. (31) provide a further possible explanation for the decreased rate of blood transfusion seen between 2018-2020. Considering all these findings, the institution of TXA into the standard management protocol of surgery for idiopathic scoliosis is warranted.

Table 4.3: Comparison of EBL in recipients of TXA versus non-recipients

Study	TXA administered		No TXA		p-value
	Number of patients	Blood loss (mL)	Number of patients	Blood loss (mL)	
Present study	21	602.38 (+/- 219.93)	15	890 (+/- 385.54)	0.018
Sethna et al. (28)	23	1230 (+/- 535)	21	2085 (+/- 1188)	<0.01
Lykissas et al. (29)	25	537 (+/- 320)	24	1245 (+/- 896)	0.027
Goobie et al. (30)	56	836 (+/- 373)	55	1031 (+/- 484)	0.02

4.7 Intra-operative use of ICS

ICS is frequently employed when a large volume of blood loss is anticipated. Likewise, the adequate use of ICS is dependent on this blood loss to be able to produce a transfusable unit of RBC. In this study, only three patients (8.33% of total patients) received this mode of treatment, as such, there were too few patients to establish a statistically significant relationship by means of inferential statistics. Importantly, while no meaningful relationship was established, all patients who received ICS had blood losses >30% of EBV. Whilst the use of intra-operative irrigation fluids could have elevated the EBL, such dramatic increases in EBL as a percentage of EBV are unlikely due to this alone. As such, all patients who received ICS were patients who were considered to be at an increased risk of blood loss. Therefore, ICS was prudently instituted secondary to the clinical foresight of the surgeon to try and manage the anticipated large blood losses. This explains why only three patients received ICS, as they were thought to be at the greatest risk of experiencing a large EBL.

Dick et al. (5) observed that the use of a multidisciplinary blood conservation program decreased EBL, and that the greatest decreases in EBL were seen with the introduction of both an antifibrinolytic and ICS. Bowen et al. (33) further validated that not only did ICS usage decrease allogeneic blood transfusion rates (6% versus 55%, $p<0.05$), but also that mean allogeneic transfusion volumes were also lower (0.4 mL/kg versus 9.1 mL/kg, $p<0.05$). Similarly, Huët et al. (31) reported that the use of ICS resulted in a lower proportion of patients receiving allogeneic blood transfusions. However, a caveat to this study was that Huët et al. (31) did not distinguish between general orthopaedic and orthopaedic spine surgery.

An infrequently cited benefit of ICS is that autologous rather than allogeneic blood is transfused (4), thus decreasing complications associated with allogeneic RBC transfusion. Furthermore, guidelines from the Association of Anaesthetists support the usage of ICS in cases where a large blood loss is expected (34). Therefore, while no beneficial effects were demonstrated in the present study with respect to the use of ICS, its use in surgery for idiopathic scoliosis would still be prudent considering the available evidence, especially when a large EBL is predicted.

4.8 Intra-operative use of UBS

One of the most recent advancements in pursuit of decreasing blood loss during corrective surgery for idiopathic scoliosis is UBS (14). This innovation has allowed surgeons to cut bone surrounding sensitive soft tissues, while the soft tissues remain relatively unaffected (14, 37). In the current study, all the patients from August 2017 onwards received the use of UBS. Hence, 18 (50%) patients received intra-operative use of UBS whilst the remaining 18 (50%) patients did not. It was found that patients who received UBS had a mean EBL of 558.33 (+/- 199.45) mL, whereas patients where no UBS was used had a mean EBL of 886.11 (+/- 353.89) mL. Furthermore, UBS was revealed to cause significant decreases in EBL; with a mean difference in EBL of 327.78 mL ($p=0.01$). This result further reinforced the cause of decline in EBL seen between 2018-2020. This emphasises that the use of both TXA and UBS likely caused reductions in EBL during this period.

Wahlquist et al. (14), and Bartley et al. (37) in their retrospective reviews similarly found that the use of UBS resulted in significant reductions in EBL (refer to Table 4.4). Additionally, Bartley et al. (37) further described that the use of UBS also resulted in a lower EBL per level fused. They reported the EBL per level fused to be 48 (+/- 30) mL in patients who received UBS versus 72 (+/- 28) mL in patients who did not (37). Bearing in mind the findings reported in the current study and the ever-expanding body of recent literature supporting the use of UBS, the importance of its integration into the surgical management of idiopathic scoliosis becomes evident.

Table 4.4: Comparison of EBL in recipients of UBS versus non-recipients

Study	UBS Used		No UBS		p-value
	Number of patients	Blood loss (mL)	Number of patients	Blood loss (mL)	
Present study	18	558.33 (+/- 199.45)	18	886.11 (+/- 353.89)	0.001
Wahlquist et al. (14)	17	771	29	1211	0.01
Bartley et al. (37)	20	550 (+/- 359)	20	799 (+/- 376)	<0.05

4.9 Additional Factors Contributing to Blood Loss

Corrective surgery for scoliosis is not only associated with large volumes of blood loss but also prolonged surgical procedures (15). As the surgical field is exposed during this time, the risk of hypothermia and the sequelae of coagulopathy remain. As such, prolonged operative times are one of the major surgery related factors postulated to increase EBL (4, 8, 15). The mean operative time in this study was 355 (+/- 75.38) minutes, with the longest procedure lasting approximately 525 minutes. Unfortunately, surgical time remains a relatively non-modifiable factor contributing to blood loss secondary to the complexity of the procedure. However, steps can be taken to optimise surgical time and therefore blood loss. These include meticulous haemostasis during the procedure, the surgical team being familiar with each step of the surgery, and lastly the aptitude of the surgeon with pedicle screw insertion (15).

It was further established in the present study that every minute spent in theatre resulted in 1.63 mL of blood loss (p=0.025). Alamanda et al. (35) correspondingly reported that every 10 minutes in surgery increased blood loss by 6.7% of the total blood volume. Hence, increased surgical time was found to be an independent predictor of blood loss (35). The importance of operative times was further highlighted by Pauyo et al. (8) in the Canadian Consensus for the Prevention of Blood Loss in Spine Surgery. The authors reported that the risk factor found to influence blood loss most profoundly was an operative time of more than five hours (8).

The number of vertebral segments fused was another factor found to significantly influence blood loss. The mean number of segments fused was 10.25 (+/- 1.87) segments. This finding is also consistent with those reported in similar literature. Hassan et al. (6) reported the mean number of segments fused to be 10 (+/- 3) segments, Chiu et al. (15) reported a mean of 9.5 (+/- 2.3) segments fused and Alamanda et al. (35) described a mean of 9.4 segments fused in their respective studies (refer to Table 4.5).

Table 4.5: Comparison of the mean number of segments fused

Study	**Number of vertebral segments fused**
Present study	10.25 (+/- 1.87)
Hassan et al. (6)	10 (+/- 3)
Chiu et al. (15)	9.5 (+/- 2.3)
Alamanda et al. (35)	9.4

Additionally, univariate linear regression showed a statistically significant association revealing that 80.24 mL of blood was lost for every vertebral segment fused (p=0.005). Parallel to this finding, Hassan et al. (6) found the EBL per segment fused to be 93 (+/- 41) mL. They further demonstrated that the number of segments fused increased the odds of requiring a transfusion and that the number of segments preoperatively planned for fusion was an indirect predictor of blood loss (6). Additionally, Lenoir et al. (17) who established the PMTSS, reported that the fusion of more than two levels was an independent predictor of blood transfusion.

Additional factors investigated in this study which showed no statistically significant association with blood loss included the scoliosis Lenke type and the Cobb angle. Importantly, while these factors did not reveal significance, they have been shown in other studies to affect blood loss. For instance, in a retrospective review by Nugent et al. (16), it was found that patients with larger curve magnitudes increased both intra-operative blood loss and surgical time. Furthermore, they reported that Cobb angles of greater than 70 degrees were predictive of RBC transfusions (16). Alternatively, Ohrt-Nissen et al. (19) found that the curve type was an independent predictor of EBL. Bearing all this in mind, future research needs to be directed towards these topics to adequately ascertain their effect on blood loss in surgery for idiopathic scoliosis.

4.10 Strategies for Reducing Intra-operative Blood Loss and RBC Transfusion

Establishing blood-saving strategies continues to be the goal of most research directed at corrective surgery for idiopathic scoliosis. This is due to the large volume of blood loss and risk of allogeneic RBC transfusions associated with it (5, 6, 15). Dick et al. (5) reported the use of a "multidisciplinary blood conservation integrated care pathway program" which integrated blood-saving strategies including: the use of TXA, ICS, restrictive transfusion triggers and preoperative Hb optimisation (5). They reported a dramatic decline in the rate of transfusion, starting from 89.2% (before any measures were introduced) to 20.1% following the institution of the integrated care pathway (5).

Similarly, Ohrt-Nissen et al. (19) implemented the perioperative "patient blood management" strategy. This was a multidisciplinary, evidence-based method aimed at reducing transfusions and improving patient outcomes (19). It included: the use of prophylactic TXA, restrictive RBC transfusion triggers, intra-operative ICS, permissive hypotension, and restrictive fluid therapy.

Interestingly, the blood-saving strategies reported by both Dick et al. (5) and Ohrt-Nissen et al. (19) had common factors including the use of TXA, ICS and restrictive transfusion triggers.

Furthermore, Fletcher et al. (10) established a best practice guideline for reducing blood loss in patients receiving posterior instrumentation for idiopathic scoliosis. In the study, 21 spine deformity surgeons reached an agreement regarding 21 of the 29 questions posed (10). Importantly, a consensus regarding routine administration of TXA, intra-operative use of UBS and restrictive Hb transfusion triggers (i.e. Hb <7 g/dL) was unanimous. Intriguingly, a consensus was not reached regarding ICS usage however, its implementation was still cautiously suggested (10).

In this study, it was found that the use of TXA and UBS were important factors in decreasing blood loss. Likewise, both the duration of surgery and the number of segments fused were also factors found to have a significant contribution to blood loss. Although there were no patients with a Hb <7 g/dL, Dick et al. (5), Ohrt-Nissen et al. (19) and Fletcher et al. (10) all quoted restrictive transfusion triggers as being beneficial in reducing unneeded RBC transfusions. Furthermore, although the current study showed no benefit when using ICS, the evidence in support of its utilisation makes it a prudent measure to institute.

Taking these findings and the results of the reviewed literature into consideration, the following recommendations are made regarding strategies to decrease blood loss and risk of allogeneic blood transfusion during posterior corrective surgery for idiopathic scoliosis:

1. Effective preoperative planning - considering the number of segments to be fused to plan for blood loss and risk of transfusion
2. Surgical time efficiency - ensuring meticulous intra-operative haemostasis and the surgical team being familiar with the surgery
3. Routine administration of prophylactic TXA
4. Standard use of intra-operative UBS - to decrease the risk of blood loss during osteotomies
5. Intra-operative use of ICS - especially when a large EBL is anticipated
6. Restrictive Hb transfusion triggers (Hb <7 g/dL) - to decrease unwarranted transfusions

With the routine institution of this multifactorial blood management strategy, the anticipation is that intra-operative blood loss and the need for allogeneic blood transfusion should decrease.

4.11 Limitations

As this was a retrospective study, it exhibited the limitations associated with this type of study i.e. difficulty with the retrieval of patient information and patient records. This resulted in an exclusion rate of 16.28% (7 patients). Another limitation was that the study was too small for good multivariate analysis amongst factors identified to predict blood loss and blood transfusion; however, meaningful conclusions from the available data could still be drawn. Additionally, the decision to transfuse was made by relying on the clinical discretion and evaluation of the anaesthetist involved in the case. Unfortunately, this determination was frequently made by different anaesthetists as they rotated through the spine theatre. This presented a potential inconsistency as different anaesthetists possibly had different clinical thresholds for RBC transfusion. Lastly, the anaesthetist/s also reported the volume of blood loss by visual estimation, which could have had the similar problem of interpersonal variability.

4.12 Recommendations

Based on the findings obtained from the study, the following recommendations are made:

1. A follow-up study with a prospective design be conducted. This would allow some of the limitations encountered in the study to be overcome.
2. Review of post-operative blood loss and transfusion requirements should also be conducted.
3. Any future study should also aim for a larger study population, to decease biases from a smaller study sample and to allow for greater precision of univariate and multivariate analysis.

Chapter 5

Conclusion

Patients undergoing posterior corrective scoliosis surgery were found to be predominantly adolescent females with a median age of 16 (IQR: 13-17) years which correlated with literature.

A review of the intra-operative blood loss demonstrated that the average EBL was 722.22 (+/-328.30) mL, which was also consistent with international literature. Additionally, most patients who underwent this procedure had a blood loss of between 15-30% of EBV.

Modifiable factors found to affect intraoperative blood loss included the use of TXA, and intraoperative deployment of UBS. Additional factors found to contribute to blood loss included the duration of surgery and the number of segments fused.

A multifactorial blood management strategy to reduce blood loss and blood transfusions during posterior corrective scoliosis surgery was subsequently formulated.

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Appendices

Appendix A: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr MHS Aftab

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M210325

NAME: (Principal Investigator)	Dr MHS Aftab
DEPARTMENT:	School of Clinical Medicine Department of Surgery Division of Orthopaedic Surgery Medical School University
PROJECT TITLE:	*Blood management strategies in posterior corrective surgery for idiopathic scoliosis*
DATE CONSIDERED:	2021/03/26
DECISION:	Approved conditionally
CONDITIONS:	Approval applies to CHBAH site only; further sites may be added on receipt by the HREC (Med) of evidence of CEO approval
SUPERVISOR:	Professor A Robertson; Drs B Milner & U Ukunda
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2021/05/19

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

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 submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **March** and therefore reports and re-certification will be due in the month of **March** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

Date 28/05/21

Appendix B: CHBAH MAC Approval Letter

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 26 March 2021

TITLE OF PROJECT:

Blood Management Strategies in Posterior corrective Surgery for Idiopathic Scoliosis.

UNIVERSITY: Witwatersrand

Principal Investigator: Dr M H S Aftab

Department: Orthopaedics

Supervisor/s : Dr U N Ukunda/Prof AJF Robertson/ Dr B Milner

Permission Head Department (where research conducted): Yes

NHRD No. GP 202103_061

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

....
Recommended
(On behalf of the MAC)
2021/03/26

....
Approved/~~Not Approved~~
Hospital ManagementDate:
Date: 30/03/2021

Appendix C: Data Collection Sheet

1. Patient demographics

    a. Patient study no.: ____________________

    b. Age: ____________________

    c. Gender: Male ☐ Female ☐

2. Patient weight: ____________________kg

3. Idiopathic scoliosis: Yes ☐ No ☐

4. Preoperative Hb: ______________g/dL

5. Post-operative Hb: ______________ g/dL

6. Lenke type: ______________

7. Main curve (cobb angle): ______________

8. Tranexamic acid administered: Yes ☐ No ☐

9. Intra-operative cell salvage used: Yes ☐ No ☐

10. Use of intra-operative bone scalpel: Yes ☐ No ☐

11. Estimated blood loss: _________________ mL

12. Red blood cell transfusion Yes ☐ No ☐

13. No. of Red Blood Cell units transfused: _________________ Units

14. Segments fused: _________________

15. Duration of Surgery: _________________