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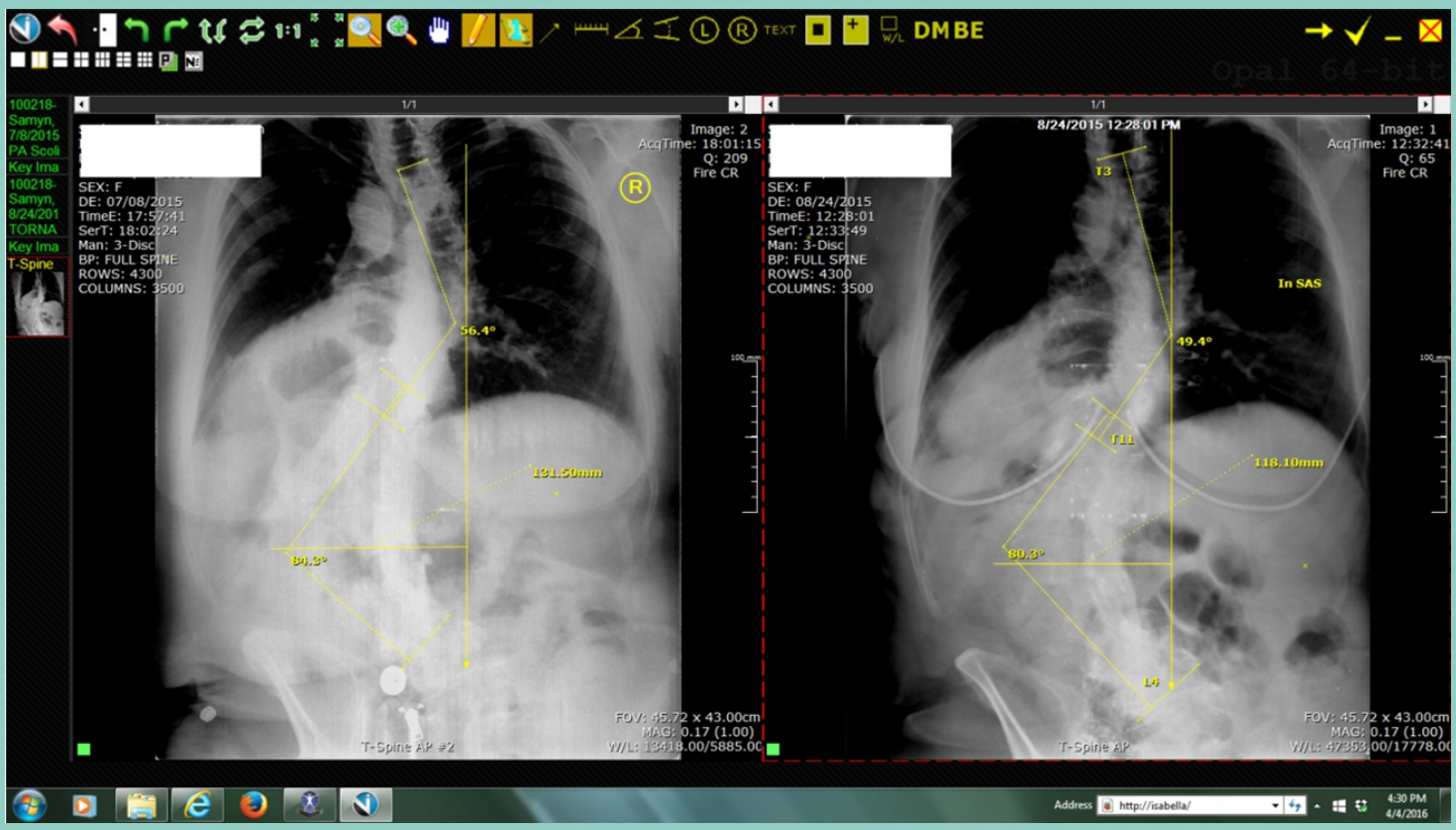

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The figure on the front cover is from the article published in International Journal of Clinical Medicine, 2016, Vol. 7, No. 4, pp. 265-269 by Mark W. Morningstar, Brian Dovorany, Clayton J. Stitzel and Aatif Siddiqui.

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Cholecystoduodenocolic Fistula: An Unexpected Intraoperative Finding, a Surgical Challenge

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Abstract

The bilioenteric fistulas, first described in 1890 by Courvoisier, are found in 0.15% - 8% of biliary tract operations. Combined fistulas involving the gallbladder, duodenum and colon are extremely rare. We presented a case of 38 year female who presented to our OPD with complaints of pain right upper abdomen for seven months in whom a cholecysto-duodenocolic fistula (Figure 1 & Figure 2) was found during surgery which was repaired primarily. Gallstone disease is a common problem in hepatobiliary system and may rarely present as cholecysto-enteric fistula. The most common type of biliary enteric fistula is Cholecystoduodenal fistula (70%). Cholecysto-duodeno-colic (CDC) fistula is a rare complication of cholelithiasis. The standard treatment of IBF is cholecystectomy and repair of the fistulous opening. Although very rare a cholecystoduodenocolic fistula should be kept as a possibility when there are adhesions between GB, duodenum and colon. Conversion to open surgery should be considered early when the anatomy is not clear to prevent iatrogenic injury.

Keywords

Fistula, Cholecystectomy, Cholecystoduodenocolic Fistula

1. Introduction

A biliary fistula is an abnormal passage or communication from the biliary system to an organ, cavity, or free surfaces. Fistula are classified as external (biliary-cutaneous) or internal (biliobiliary, bilioenteric, bronchobiliary) [1]. The bilioenteric fistulas, first described in 1890 by Courvoisier, were found in 0.15% - 8% of biliary

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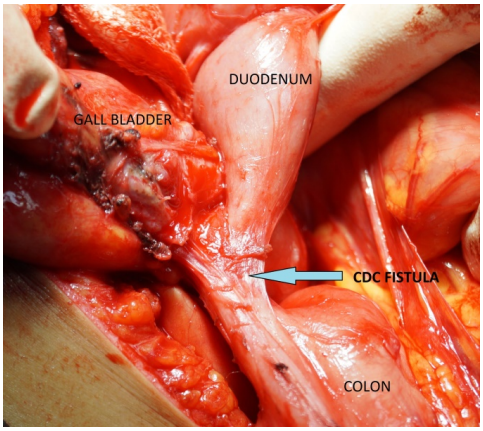

Figure 1. Image showing Cholecysto-duodeno-colic (CDC fistula-shown by arrow).

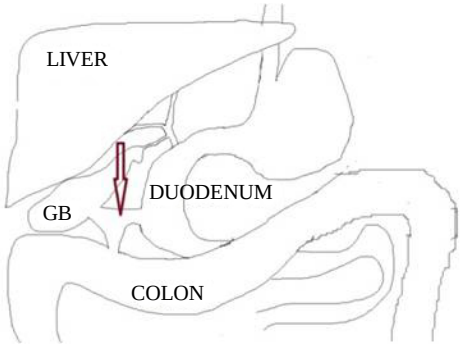

Figure 2. Representational diagram of Cholecysto-duodeno-colic fistula (arrow).

tract operations. Out of which about 70% are Cholecystoduodenal and 8% to 26.5% are cholecystocolic and usually located at the hepatic flexure, with higher incidence in the elderly and in women [2]-[5]. Internal biliary fistula (IBF) is associated with chronic cholelithiasis in 90% of the cases. Preoperative diagnosis of IBF is difficult [6]. As the symptoms of IBF include abdominal pain, fever, nausea, vomiting, flatulence, fat intolerance, diarrhoea and weight loss, which are all non-specific and seen in most gastrointestinal pathologies, the diagnosis is often not suspected preoperatively [7]. The diagnosis is usually made preoperatively [8]-[10].

Cholecystocolonic fistula (CCF) is a late complication of long-lasting gallstone disease and is found in roughly 1 in every 1,000 cholecystectomies. It is the second most common cholecystoenteric fistula after the Cholecystoduodenal [11]-[13].

Symptoms of CCF are usually minimal and/or non-specific, and preoperative diagnostic tools often fail to show such a rare condition, hence diagnosis is often achieved intraoperatively [14] [15].

Combined fistulas involving the gallbladder, duodenum and colon are extremely rare [16]. A double communication of the gallbladder with both the duodenum and colon is rare in this condition, only five previous cases having been recorded in the English literature (Doromal, Estacio and Sherman, 1975; Dowse, 1963; Pitman and Davies, 1963; Shocket, Evans and Jones, 1970) [17].

Objective: Cholecystoduodenocolic fistula which is one of the rarest complications of gall bladder stones can be difficult to diagnose preoperatively and needs an early suspicion intraoperatively to prevent injury to adjacent structures.

2. Case Report

We report a case of 38 year female who presented to our OPD with complaints of pain right upper abdomen for seven months. Pain was of moderate intensity continuous and non-radiating. Patient had no history of jaundice

and intestinal obstruction. There was no history of any abdominal surgery in the past. Patient had no history of any bowel pathology. There was no other significant complaint. General physical examination was normal with no signs of any nutritional deficiencies. Local examination of the abdomen was normal with no palpable organomegaly and no free fluid. Patients heamoglobin was 13.4 gm/dl, total bilirubin was 0.5 mg/dl, alkaline phosphatase was 48 IU/L. Ultrasonography (USG) abdomen revealed contracted Gall bladder (GB) with a single calculus in neck region with 3.5 mm wall thickness. CBD was normal. Patient was worked up for laparoscopic cholecystectomy.

Laparoscopic cholecystectomy was done after taking down adhesions. Callot's anatomy was found to be distorted. After meticulous dissection the duodenum and transverse colon were found adherent to gall bladder. With high suspicion of a Cholecystoduodenal fistula and non-progression of surgery by laparoscopy, it was decided by surgical team to convert the procedure to open. GB was dissected by fundus first method. A cholecysto-duodenocolic fistula (CDCF) (**Figure 1**) was found as the adhesions between GB and Duodenum and colon were taken down by sharp dissection. The fistulous tract was excised. Colon repaired primarily and duodenum was repaired by omental patch. Cholecystectomy was completed and abdomen closed. Postoperative period was uncomplicatedand patient was discharged on sixth post-operative day. Patient has been under regular follow up since last 3 months and is doing fine.

3. Discussion

Gallstone disease is a common problem in Indian subcontinent. It can present as acute cholecystitis, gall stone pancreatitis, obstructive jaundice, gallstone ileus or cholecysto-enteric fistula. Although many patients will be asymptomatic and may present as an incidental finding on imaging done for some other reason.

The most common type of biliary enteric fistula is Cholecystoduodenal fistula (70%) followed by cholecystocolic fistula (8% - 26%) [2]-[5] and the least common cholecystogastric fistula. The reported incidence of internal biliary fistulas is about 2% of total biliary diseases [18]. The most common cause is pressure necrosis due to an impacted gallstone usually in the neck of gallbladder, which gradually erodes into the duodenum [19].

Cholecystoduodenocolic (CDC) fistula is a rare complication of cholelithiasis. Only 21 examples had been reported up to 1984 [17]. High index of suspension might help to diagnose it preoperatively.

The standard treatment of internal biliary fistula (IBF) is cholecystectomy and repair of the fistulous opening [20]. Modern techniques in laparoscopy should allow safe laparoscopic cholecystectomy, even for patients with cholecystoduodenocolic fistula. The fistulous tract can be divided by an endo-GI stapler. It may be safer to convert to open surgery when the anatomy is not clear or the expertise is not available.

4. Conclusion

Although very rare a cholecystoduodenocolic fistula should be kept as a possibility when there are dense adhesions between gall bladder, duodenum and colon. Conversion to open surgery should be considered early when the anatomy is not clear to prevent iatrogenic injury.

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Radiographic, Pain, and Functional Outcomes in an Adult Post-Fusion Patient Using a Scoliosis Activity Suit: Comparative Results after 8 Months

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Abstract

There are few conservative treatment options for adult patients with idiopathic scoliosis who are status post-fusion surgery. These typically include pharmacologic pain management, epidural injections, and generalized CAM treatments such as massage and chiropractic manipulation in the non-fused areas of the spine. The purpose of this study was to compare the post-treatment results in an adult post-fusion patient who wore a scoliosis activity suit for 8 months. Pain was evaluated using a quadruple visual analog scale (QVAS), while function was measured using an SRS-22r questionnaire. After 8 months of wearing the scoliosis activity suit, her pain scores improved, here SRS-22r improved, and a significant correction in radiographic Cobb angle was observed. This case report is the first to document a Cobb angle change in an adult patient wearing a scoliosis activity suit who is status post-fusion. Given that pain and dysfunction are primary reasons for scoliosis treatment in the adult population, more studies need to address the disparity between available treatments for adult scoliosis and the incidence of adult scoliosis, especially in the post-menopausal population. Future prospective studies should consider evaluating treatment effects of this suit using intent-to-treat methodology.

Keywords

Chiropractic, Pain, Rehabilitation, Scoliosis, Spine

*Corresponding author.

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1. Introduction

Scoliosis is a lateral curvature of the spine exceeding 10 degrees as measured by Cobb's angle, and is thought to occur in 2% - 3% of the adolescent population annually [1]. According to the National Scoliosis Foundation [2], 38,000 spinal fusion surgeries are performed each year for progressive idiopathic scoliosis. Although this has been the treatment of choice for decades, there have been recent reports calling the safety and necessity of scoliosis fusion surgery into question [3]. Unfortunately, many complications can occur years after the initial surgery [4]. In a study of patients who had Harrington rod surgery for adolescent idiopathic scoliosis, 40% of these patients were classified as legally disabled 16.7 years after the surgery [5]. Since spinal fusion surgery does not substantially improve pain levels, some authors recommend [6] more judicious use given the high rate of complications.

Given that post-fusion patients still experience pain after surgery [7], adult patients are seeking more opportunities for pain management. Recently, Morningstar *et al*. have published preliminary reports on a scoliosis activity suit for adult scoliosis treatment [8] [9]. They report both radiographic and pain improvements in adult patients wearing this suit for up to 18 months. Although radiographic Cobb angle changes are logically unlikely in post-fusion patients, Morningstar and Joy demonstrate a Cobb angle correction in an adult post-Harrington fusion patient who participates in a chiropractic rehabilitation treatment [10]. This case report summarizes the findings and treatment of an adult post-Harrington fusion patient. Outcomes are reported after wearing a scoliosis activity suit for 8 months.

2. Case Report

A 59 year old female presented to an integrative medicine clinic with a history of adolescent idiopathic scoliosis diagnosed at age 13. The patient could not recall her initial Cobb angle measurement. She subsequently had Harrington rod instrumentation at age 19, which corrected the curve to 25˚. She had a revision surgery one year later due to pseudarthrosis, and a second revision surgery performed in 1992 due to hardware failure. The hardware was removed during this third surgery. Approximately 5 years after the third surgery, the patient recalled having back pain and right-sided sciatica with radiation from the right sacroiliac joint into the right posterior thigh above the knee. The pain was present at least 75% of the day most days. She had been using medicinal marijuana to help control her pain levels. She reports that the medicinal marijuana, along with turmeric allowed her to be more functional than compared to prescription pain medications.

As part of her initial intake paperwork, the patient completed a quadruple visual analog scale (QVAS) [11] and a revised Scoliosis Research Society 22 (SRS-22r) questionnaire [12] to quantify pain levels and quality of life. Her baseline QVAS score was an 80 out of a maximum score of 100. Her SRS-22r scores for each domain were as follows: Pain: 6/25, Function: 12/25, Self-image: 10/25, Mental health: 17/25, and Management satisfaction: 2/10 for a total score of 47/110. Baseline radiographic images in July of 2015 showed a Cobb angle of 84˚ from T11-L4 with an apex of L1/L2, and a 56˚ curve from T5-T11, apex T8.

3. Intervention and Outcomes

Since the patient's main purpose in seeking treatment was pain relief and functional improvement, the patient was scheduled to begin a course of therapy using the scoliosis activity suit. The patient presented for a trial fitting of the scoliosis activity suit. The activity suit is a neoprene wrap-based activity suit. The activity suit is composed of 4 separate pieces. The main piece, the Anchor, is the wrap that fits around the patient's thigh. The Lumbar piece attaches directly to the Anchor, and their configuration is dependent upon the location of the lumbar or thoracolumbar curvature. The third piece is called the Torso piece, and looks like a half-tank top shirt that acts upon the thoracic curvature. The fourth and final piece, or set of pieces, is the tension straps. The tension straps connect each of the first three pieces together in a rotational pattern, which introduces a variable amount of rotational force into the patient, to which he or she must react. These tension straps may be long or short. The longer tension straps are more elastic and provide more rotational resistance to which to resist. The activity suit was designed with the goal of creating a rotational resistance to which the postural reflexes and associated axial musculature must adapt. These rotational adaptations are measurable via visual posture analysis as well as comparative radiography.

Once a configuration was applied that produced a positive postural change, the patient was asked to wear it in the clinic while walking for 20 minutes. After that an in-suit radiograph was taken to evaluate correction. **Figure 1**

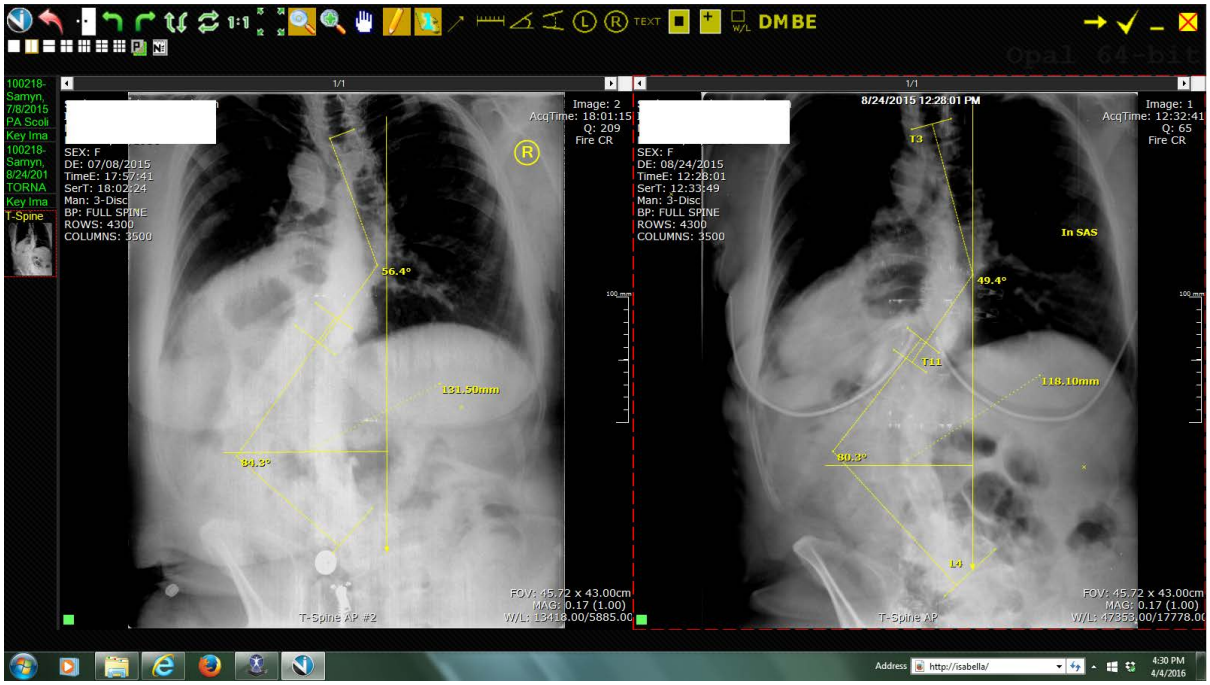

Figure 1. An illustration of the radiographic change while wearing the scoliosis activity suit.

shows the in-suit correction illustrated. The Cobb angle of the primary lumbar curvature mildly reduced to 80˚, while the thoracic curve reduced to 49˚. After instructing the patient on replicating the scoliosis activity suit's application, she was instructed to wear the suit for 1 hour twice daily, particularly around times of the day where she would be the most active. The patient followed up one month later to begin some basic at-home activities to perform while in the suit. These activities included some basic range of motion exercises, as well as some supine core strengthening exercises.

The patient was then instructed to follow-up in another month for additional exercises. During this follow-up, the patient, of her own volition, increased her activity suit time to 2 hours per session twice daily due to the pain relief she received while wearing it. After instructing her on additional core stability exercises, the patient was asked to follow-up 6 months later.

At her 6-month follow-up, the patient had completed follow-up QVAS and SRS-22r questionnaires for comparison. Her 6-month QVAS score was a 47/100 for a 59% reduction in pain. Her SRS-22r follow-up scores for each domain were as follows: Pain: 14/25, Function: 19/25, Self-image: 14/25, Mental health: 20/25, and Management satisfaction: 8/10 for a total score of 47/110, This is improved overall by 75/110, equating to a 60% improvement. A follow-up radiograph was obtained of the patient, prior to which the patient had not worn the scoliosis activity suit for 24 hours. **Figure 2** illustrates this follow-up radiograph. The lumbar curve measured 63˚, while the thoracic curve was reduced to 38˚.

4. Discussion

Since chronic pain and disability can significantly impact post-fusion scoliosis patients, it is imperative to explore new ways of helping this patient population. Given that this particular patient had her hardware removed by the time she presented for the treatment described herein, we cannot apply these results to other post-fusion patients necessarily. Due to the difference in surgical hardware and techniques, these results may not hold true for patients with pedicle screw instrumentation, Cotrel-Doubousset instrumentation, Luque instrumentation, etc. This report only outlines the treatment of a patient who underwent Harrington rod instrumentation as a young adult. It is unknown if or how the scoliosis activity suit could impart changes in the Cobb angle measurement in a patient who had their hardware in place at the time of scoliosis activity suit application. However, future studies should consider that this patient population may only want/need quality of life and pain improvements for a given treatment to be considered successful for these patients.

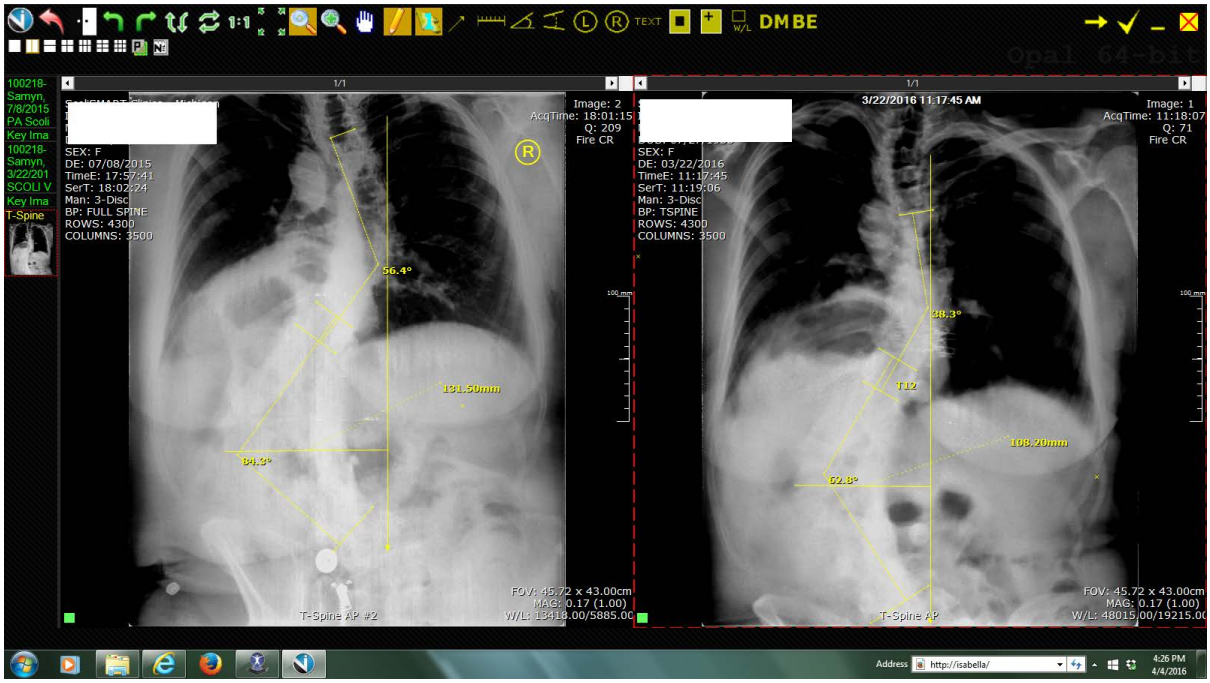

Figure 2. Radiographic changes after wearing the scoliosis activity suit for 8 months.

The amount of Cobb angle change in this case was significant. Our theory is that this could only be possible in someone with the hardware removed. We don't know what type of change, if any, would be possible in an adult of this age her still had her hardware in place. However, Morningstar and Joy were able to also get Cobb angle correction in an adult patient who did have Harrington instrumentation still in place. Both of these cases are single examples, and therefore their results cannot be applied broadly.

5. Conclusion

After wearing a scoliosis activity suit for 8 months, a 59 year old adult post-fusion female patient obtained clinically significant changes in self-reported pain and quality of life scores, as well as corrections in her thoracic and lumbar scoliosis Cobb angles. More research on scoliosis treatment for this particular patient population was needed, in light of the incidence of surgical complications associated with spinal fusion surgery.

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Perioperative Nursing Management of an Animal Model of Axial Flow Blood Pump Implantation

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Abstract

Objective: This study aimed to explore the characteristics of perioperative nursing of experimental goats using self-made axial-flow blood pump implantation and provided theoretical nursing knowledge and practice-based evidence for the clinical application of domestically manufactured artificial cardiac pumps. Methods: Seven experimental goats were used in this study, three for pre-testing and four for the formal experiments. According to the surgical requirements for axial-flow blood pump implantation into the cardiac apex, we creatively designed and made a series of highly practical animal surgical instruments including a composite disassemblable bed for experimental animal transferring and monitoring, a multifunctional animal surgery bed, and portable medical supporting equipment. We also applied for two national invention patents and one utility model patent. Active measures were taken to ensure careful preparation before surgery, close collaboration during surgery, and effective management of complications after surgery. Results: Two of the four experimental goats died during surgery because of a massive hemorrhage caused by distal anastomotic failure and air embolism-induced cardiac arrest caused by air leakage from the outlet into the heart due to poor connection of the auxiliary pressure tap (used to measure left ventricular pressure). The mean survival time of the remaining three experimental goats was 22.7 hours. Conclusion: This study was the first to systematically and comprehensively investigate the perioperative nursing management of axial-flow blood pump implantation using animal models. These findings could greatly promote further clinical applied nursing research of self-made artificial cardiac pump implantation in experimental goats.

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Keywords

Axial-Flow Left Ventricular Assist Devices (LVADs), Goats, Perioperative Nursing Management

1. Introduction

Current clinical evidence shows that heart transplantation is the treatment of choice for severe heart failure. However, the demand for healthy donor hearts greatly outnumbers the supply. According to incomplete statistics, there are approximately 1.5 million patients with end-stage heart failure in China, of which, the majority die while awaiting transplantation due to the shortage of donor hearts. Most of these patients can survive or undergo transplantation surgery if they are provided with suitable circulatory support [1]. In western countries, artificial hearts have been clinically used as bridge-to-transplant devices, which can partially or completely replace defected hearts and restore their biological functions [2]-[10], thus enabling patients to safely pass the waiting period prior to heart transplantation.

Research on ventricular assist devices (VADs) in our country has a late start, and dozens of research institutes have conducted studies on axial-flow VAD in recent years [11] [12]. However, the related studies are still at the animal experiment stage, and various technical difficulties and post-operation complications remain unsolved. In May 2010, our institution began to study and develop implantable axial-flow left ventricular assist devices (LVADs) and eventually completed experiments on seven goats.

Focusing on nursing-based medical care, this study systematically and comprehensively explored perioperative nursing management of self-made axial-flow blood pump implantation in experimental goats. Participation of nursing personnel in this animal study of artificial cardiac pumps allows us to obtain important clinical nursing insights. Therefore, this study can provide theoretical nursing knowledge and practice-based evidence to accelerate the clinical application of domestically manufactured artificial cardiac pumps. Animal Study of Perioperative Care *in vivo* homemade axial implants artificial heart pump.

2. Patients and Methods

2.1. Experimental Animals and Preparations

We choose the Boer-Hybrid female goats as animal model for several reasons: the heart volume of goats about 40 kg was similar with human, which was clear to operate; the Boer-Hybrid was tame to test and collect blood for the researchers. The seven goats were average two years and have a weight between 30 to 48 kg from sheep farm. Researchers were fixed for establishing emotion with animal, which was beneficial for the nursing [13]. The experimental goats were detected and expelled worms. First of all, preparing 200 or 300 ml goat blood storing in the 4˚C - 8˚C refrigerator preoperative. Secondly, detect the electrocardiogram, body temperature, routine blood, routine urine, routine coagulation, D-D2, free hemoglobin, blood sugar and serum biochemistry. Thirdly, preoperative skin preparation and bathing for experimental goats before one day. We shaved the goat body hair when skin preparation for operation and the fixed pipeline. We also make up number on the goats for saving and detecting the experimental materials (**Figure 1(a)**). Finally, fasting for 24 hours and forbidden drinking for 12 hours before operation. [14] by right lateral given atropine 0.03 mg/kg and ketamine 3 mg/kg (intramuscular) before anesthesia. After that, jugular vein catheter was installed and the goats were given the ketamine and propofol (1:2) to maintain the anesthesia. Meanwhile, we also use the homemade laryngoscope to find the trachea opening and inserted the pipe. Finally we pull out the guidewire to inject about 5ml air to fix the pipe. We connected the anesthesia ventilator to give the isoflurane through the pipe.

2.2. Experimental Instruments and Equipment

The apical axial flow device (**Figure 1(b)**) [15] has the control portion in vitro and implanted portion *in vivo*. The implanted portion was cylindrical axial flow which was the total volume of 42 ml, the weight of 110 g, outside diameter of 26 mm and a 75 mm length. We used good compatibility medical stainless steel or titanium as a wall, which was a 18.4 - 20.6 mm diameter and a 12 mm diameter grafts guide at the entry and exit ports. The specific parameters are 11000 r/min speed, 100 mmHg press, 5 L/min flow, 12W power and 13 mm diameter.

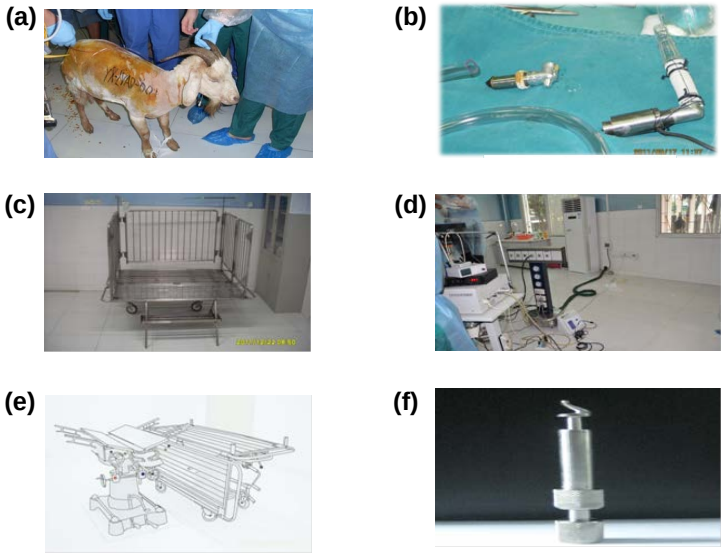

Figure 1. A. Goats; B. The apical axial flow device; C. Removable modular transporter animal care bed; D. Portable medical devices; E. Multiple-functional animal surgery bed; F. Spiral-myocardial punchers.

The vitro control portion was made up of power battery and control circuit which work similar with the common brushless direct current motor. The speed was regulated by input voltage [16].

Experimental surgical instruments were prepared by the goats' weight and height for the deep intro-thoracic operations. The equipment included anesthesia machine (NARKOMED2C12662), multi-parameter anesthetic gas monitors (Vamos), Electrocardiogram (Agilent CM2001, RSM-4101K, MIHON KOHDEN, Japan), and ACT measuring instrument (ACT II, Medtronic Inc, America). There were also several innovative design of equipment such as removable modular transporter animal care bed [17] (National Invention Patent No.ZL 201210042605.8, **Figure 1(c)**), portable medical devices [14] (National utility model patent No.ZL 2011203-25472.6 **Figure 1(d)**), multiple-functional animal surgery bed [18] (National utility model patent No. ZL 201110374405.8, **Figure 1(e)**) and spiral-myocardial punchers (**Figure 1(f)**) [19].

We give the implementation of catheterization or bladder puncture, gastrostomy to decompression detection of invasive arterial blood pressure, electrocardiogram, oxygen saturation, and serum biochemical indices. In order to make the activated clotting time (ACT) to 400s we give the intravenous heparin 1.5 mg/kg. We also give the Pioneer-5 1.5 mg and dexamethasone 10 mg preoperatively. After preparation we implemented the left ventricular assist device (LVAD) [20] [21] at the apical and the exit of blood pump was connected with descending aorta by artificial blood vessels. The wire of blood pump was exported from chest incision and placed chest drainage device. By this way we established the left ventricular-LVAD-descending aorta circulation loop (**Figure 2(a)**): Thoracotomy at the left fourth intercostal space; (**Figure 2(b)**): The side wall of the descending aorta clamp clip; (**Figure 2(c)**, **Figure 2(d)**): Descending aorta connected with artificial blood vessels; (**Figure 2(e)**, **Figure 2(f)**: Apical drilling; (**Figure 2(g)**, **Figure 2(h)**): Implement LVAD at apical and detect the device data.

2.3. Experimental Drugs

Hydroxyethyl starch, dexamethasone (HuBei Tian-Yao Pharmaceutical Co., Ltd., China), tranexamic acid (Chongqing Levin US Pharmaceutical Co., Ltd., China), ketamine (Fujian Gu-Tian Pharmaceutical Co., Ltd., China), propofol injection (AstraZeneca Pharmaceutical Co., Ltd., China), Lidocaine (Shandong Hua Lv Pharmaceutical Co., Ltd., China), potassium chloride (Shanghai Hai Hong Pharmaceutical Co., Ltd., China), dicynone (Hubei Tian Yao Pharmaceutical Co., Ltd., China), dopamine (Shanhai He Feng Pharmaceutical Co., Ltd., China), nitroglycerin (Helan Run Hong Pharmaceutical Co., Ltd., China), heparin (Shanghai No. 1 Biochemical Pharmaceutical Co., Ltd., China), protamine (Shanghai No. 1 Biochemical Pharmaceutical Co., Ltd., China), isoflurane (Shanghai Yapei Pharmaceutical Co., Ltd., China).

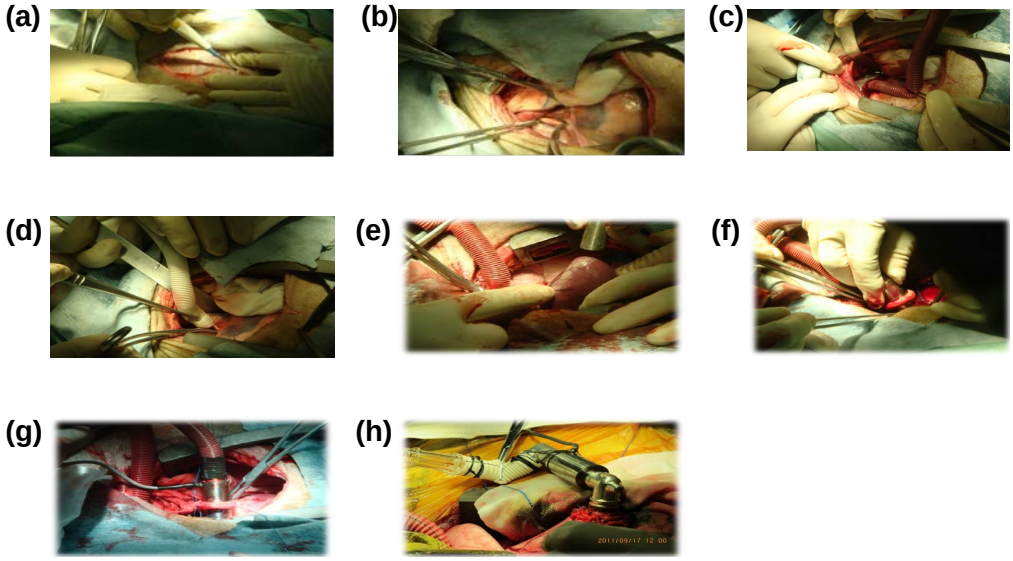

Figure 2. A. Thoracotomy at the left fourth intercostal space; B. The side wall of the descending aorta clamp clip; C, D. Descending aorta connected with artificial blood vessels; E, F. Apical drilling; G, H. Implement LVAD at apical and detect the device data.

2.4. Method: Perioperative Nursing Management

2.4.1. Preoperative Nursing Management

In order to avoid infection of experimental animals the operation room was cleaned totally and used chlorine disinfectant to wipe flawless and operation table. The operating room was sealed sterilization with ozone sterilizer one day before operation. We take air disinfection with ultraviolet circulation wind. The mops were decontamination for 30min and then air-dry [22].

2.4.2. Intraoperative Nursing Management

After general anesthesia we give the goats' conventional skin disinfection and paste electric knife negative plate which was fixed by elastic bandage. In the process of operation we pay close attention to the rate, press, oxygen saturation, breath and salivation. We also reported the parameters for the doctors to regulate the blood pump [23]. When the speed reached to 8000 - 10000 r/min and the flow reached to 4 - 5 L/min the blood pump could maintain the goats' normal pressure (**Figures 3(a)-(c)**).

2.4.3. Postoperative Nursing Management

1) Observe basic vital sign

After anesthesia the body temperature of goats was usually low which easily induced arrhythmia and unstable blood pressure. The temperature of goat named number 1 was 36 Celsius degree. Therefore we sew body-warmers (**Figure 3(d)**) and used the air conditioning to maintain the goats' body temperature up to 38 - 39.6 Celsius degree. We observed the postoperative vital signs including ruminant, petechial, hematoma and wound [24], and also detected the active clotting time (ACT) regularly, D-D2, free hemoglobin, serum biochemistry and oxygen content for diagnosis to provide the clue.

2) Blood pump management

Because the blood bump was easily dropped we used about 10 centimeter bandage to fix it for two weeks avoiding its pipe anfractuous. Postoperatively we observed the speed, curve and current of blood pump. According to the experimental data the blood pump could maintain the animal for the normal blood pressure when the speed reached to 8000 - 10000 r/min. When the speed was under 6000 - 7000 r/min it cued the thrombus were formed in the pump. At this time we needed to up-regulate the speed to 12000 r/min about 5 to 10 min to wash the thrombus.

3) Haemorrhage management

In the four cases of experiments *in vivo* one of them was dead because of the distal adverse anastomosis. In

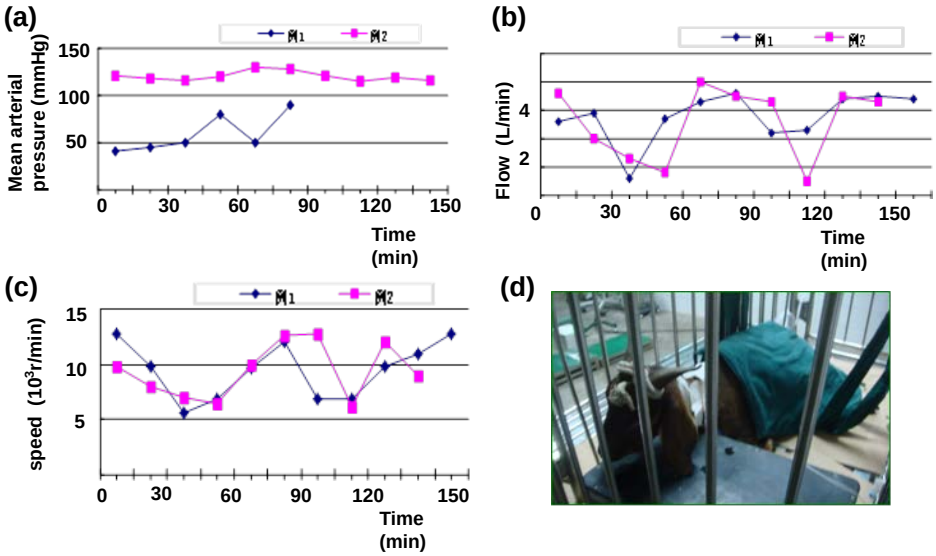

Figure 3. A. 2 cases of experimental goat left heart assist device installed in mean arterial pressure; B. 2 cases of experimental goat left heart assist device installed in the blood pump flow; C. 2 cases of experimental goat left heart assist device installed intraoperatie blood pump rotate speed; D. Body-warmers.

the early postoperative we also detected the activated clotting time (ACT), hemoglobin (Hb) and blood platelet to determine whether given anti-coagulation. Because the goats were monitored on the ground we manufactured a new bed which was easily assembled and transport. In order to avoid hemorrhoea in operation we also developed spiral myocardial perforator (**Figure 1(f)**. By this way there was little blood effusion when operation.

4) Hematolysis management

After operation free hemoglobin (F-HB) and lactate dehydrogenase (LDH) of the second goat were higher than preoperative; after blood pump work we collected urine at several stages and found hematoglobinuria which demonstrated the blood pump may led to mechanical hemolysis (**Table 1**). The nurse point was to monitor the goats' hematuresis, hematochezia, F-HB and LDH.

5) Heart and kidney management

After operation the first and second goats appeared cough, ruminate, hydrosome and ears droop. Out data (**Table 2**) show that the urea and creatinine increased in the first and second goat, which demonstrated the goats have the functional damage of heart and kidney.

6) Respiratory system management

The fourth goat was dial out organ intubation and appeared salivate and respiratory arrest. By emergency intubation the breath of goat was recovery, but unfortunately the goat was dead after postoperative several hours. We though the goat with anesthesia after operation should not extubate early. By analyzing our data we concluded the best time for the extubation was ten minutes after anesthesia and spontaneous breathing. We also pay attention to the orthostatic to keep air tube clear and clean the oral nasal secretions.

7) Nutrition support management

After postoperative one hour we only gave water under conscious. Then we feed the goat with fresh leaves to enhance appetite. After postoperative twenty-four hour we feed the goat with green grass which was chopped to improve digestion. According to twenty-four hour intake the goats were also given intravenous rehydration, amino acid and intralipid to supply energy [25].

8) Infection prevention and control maintenance

The infection of goats may be due to air pollution in the operating room or intensive care unit, but also due to pollution from the staff operation or goats' urine. To prevent infection from contamination during invasive procedures in the course of nursing, large doses of antibiotics were early used (cefazolin sodium 1.5 mg + dexamethasone 10mg i.v. before operation, and cefazolin sodium 15 mg/kg q6h i.v. after operation). Furthermore, adequate drainage of intrathoracic bleeding was noted and dressings were replaced in time for avoiding occurrence of local blood congestion [26]. The Goats blood sugar was positively controlled in preoperative andposto perative,

Table 1. The plasma free hemoglobin (mg/L) and lactate dehydrogenase (u/L) were measured before and after operation in 2 patients with experimental left ventricular assist device.

Goat	Index	Preoperative	Postoperative (hour)						
No			5 h	10 h	15 h	20 h	25 h	30 h	35 h
1	F-HB	21.6	343.4	139.5	138.8	241.3	214.6	53.6	43.8
	LDH	357	-	-	-	-	959	--	-
2	F-HB	36.4	-	3142.3	-	1969.6	-	-	-
	LDH	206	-	-	-	2042	--	-	-

Table 2. Changes of renal function before and after operation in 2 cases of experimental goats with left ventricular assist device (mmol/L).

Goat No	Index	Preoperative	Postoperative	ostoperative
			Day 1	*Day* 2
1	Urea	8.15	16.92	19.76
	Creatinine	45.00	69.00	69.00
2	Urea	8.35	16.01	-
	Creatinine	35	173.00	-

notes: Urea normal: **1.87 ~ 8.3 mmol/L**, creatinine normal: **45 ~ 84 mmol/L.**

and energy materials were supplied in postoperative. A good environment should be maintained by clearing goat droppings and disinfecting air regularly (indoor ventilation twice per day and circulating air ultraviolet disinfection three times per day).

9) Environmental maintenance

a) Temperature and humidity, as two of important factors that influence animals thermal equilibrium, were adjusted respectively at 12˚C - 24˚C and 40% - 70% according to the physiological requirements of goats. b) Light intensity and photoperiod could affect the physiology and behavior of animals [27]. To avoid glare on animals, ICU installed infrared camera system, using natural light during the day, and using infrared ray at night. c) Goats, as ruminants, could not be good rumination in the case of distraction that affects nutrient absorption and utilization. So the medical staff and workers should keep "four light" [28] (speaking light, operating light, closing light, walking light) during operation. Staffing should be reasonable, and the noisy and sharp metallic sound should avoid when transport the equipment [29].

2.5. Experimental Data Collecting

(1) LVAD detector recorded the parameters of blood pump concluding speed, current and curve.

(2) Before operation we detected regular biochenmistry. After operation we regularly detected ACT, D-D2, F-HB, blood sugar, serum biochemistry.

(3) After operation we recorded cycle indicators of goats including temperature, puls, breathing, oxygen saturation, angiosthenia, left ventricular pressure, central venous pressure.

3. Results

Death of an experimental goat was defined as its circulatory or pulmonary system ceasing to function for ≥6 minutes. The animal was dissected immediately after its death and the blood pump was removed. The interior as well as opening and exit passages of the blood pump were checked for thrombus formation. Vital organs such as the heart, lungs, liver, kidneys, and spleen were visually inspected for infarction-associated pathological changes and then subjected to pathological sectioning examination. Seven experimental goats were used in this study, three for pre-testing and four for the formal *in vivo* study. One goat in the formal study died during surgery of a massive hemorrhage caused by a distal anastomotic failure and another goat die for air embolism-induced cardiac arrest caused by poor connection of the auxiliary pressure tap (used to measure left ventricle pressure) that led to air leakage from the outlet into the heart (no post-surgical observation data available). The mean survival

time of the other three goats was 22.7 hours (experimental goat ④ only survived for 7 hours and no post-surgery observation data were available). The autopsy results showed that the apically inserted assist device was loosely connected to the artificial blood vessel in experimental goat ④. Experimental goat ② had a broken cardiac catheter that was used to measure left ventricular pressure and died of a postoperative hemorrhage. In experimental goat ①, the blood pump automatically stopped working at postoperative hour 30. This could be related to thrombus formation within the blood pump, failure of anticoagulant therapy, or wearing of the blood pump–bearing system (**Table 3**).

4. Discussion

4.1 Issues and Improvement Measures in Nursing Management of Axial-Flow Blood Pump Implantation in Animals

The sample size of this study was small and the average survival time of the experimental animals was 22.7 hours. However, we managed to summarize the nursing issues encountered during the experimental surgical process and developed specific improvement measures to provide clinical experience for the animal studies of blood pumps in China.

First, one goat died of a hemorrhage during surgery because of distal anastomotic failure. Hence, it was crucial that the surgeon was familiar with the anatomical structures of experimental goats before surgery. During surgery, the surgeon should pay attention to the connection of the distal blood vessels to the pump as well as the auxiliary pressure tap (used to measure left ventricle pressure). The nurses' responsibilities included preparing appropriate surgical instruments according to the experimental goat's chest depth before surgery, being familiar with the surgical procedures, collaborating closely with others during the operation, and monitoring the postoperative drainage volume of the pleural fluid.

Second, our observation of the four goats suggested that red blood cell damage, hemolysis, and thrombosis were the major postoperative complications. Wound bleeding was observed despite the administration of heparin injections and immediate dosage adjustments according to the activated coagulation time, 25-hydroxy-vitamin D-D2, and free hemoglobin levels. Necropsy revealed blood clot formations within the blood pumps and near the connection points between the distal blood vessels and blood pumps. Blood and blood clots had accumulated in the chest cavity. Continuous monitoring showed an increased free hemoglobin level in all animals after surgery and varying levels of hemoglobinuria. These observations could be attributed to bleeding from the wounds and anastomotic sites as well as thrombosis and hemolysis associated with wearing of the axial blood pump-bearing system. Therefore, it was necessary to improve the design of the axial-flow type II blood pump. Moreover, extra attention should be paid to the nursing management of complications such as embolism, especially bleeding monitoring and treatment and anticoagulant therapy.

Third, study data had shown that LVAD implantation complications included infection and multiple organ failure. Thus, emphasis should be put on the management of heart failure complications and monitoring hemodynamic changes during postoperative care. To reach optimal cardiac output, frequent pump pressure adjustments should also be made. Observation and recording of device parameters could provide information about device improvement and development.

Table 3. Causes of death of the four experimental animals.

No.	Survival time (h)	Cause of death
1	41.7	The blood pump stopped working due to thrombus formation
2	19.5	Cardiac catheter inserted into the left ventricle was broken, leading to a massive postoperative hemorrhage
3	Died during surgery	Distal anastomotic failure leading to a massive hemorrhage during surgery
4	7	Loose connection between the assist device and the artificial blood vessel leading to a massive postoperative hemorrhage

Fourth, problems encountered during LVAD implantation in experimental goats and the corresponding solutions could guide future studies. During this study, the nursing personnel participated in preoperative discussions to understand the anesthetic and surgical regimens. After surgery, they were also involved in the autopsies of the experimental goats and the discussions of the causes of death with the surgeons and veterinarians. Issues encountered in each experiment were summarized to make improvements and increase work efficiency in the subsequent experiments.

Fifth, all nursing procedures of each experiment should be documented in a timely, subjective, accurate, authentic, complete, and concise manner. For accountability, all record data sheets should be signed and dated by those who wrote or modified them. All experimental records and relevant information of the experimental animals should be compiled and documented accordingly within 72 hours after each experiment for analysis, ensuring the traceability of all data.

4. 2. Animal Ethics

Animal nursing management affects surgical completion and experiment results accuracy. To improve animal cooperation and achieve a stable success rate, attention to animal welfare is of great significance. Thus, animal care units for experimental goats should be established according to their physiological characteristics. Prior to surgery, nursing personnel should initiate and develop a relationship with animals as early as possible to minimize their unfamiliarity with their surroundings and rejection of humans. This can reduce the possibility of experimental failure related to factors such as noncooperation and tubes slipping off.

4. 3. Effective Management and Cost Control

This experiment has a high requirement of device number and quality, thus requiring a high investment cost. To effectively reduce the cost, we designed and made our own experimental equipment and instruments that met the needs of the animal cardiac experiment and could be further promoted in other animal and clinical studies. Nursing personnel who will participate in such studies should pay attention to equipment maintenance and minimize possible damage, thus contributing to cost control.

4.4. Prospective Insight and Hypothesis for Human Application

Here we summarized our nursing management experience and further obtained some clinical insight on axial-flow blood pump implantation based on seven animal experiments. If clinically proven for use, axial-flow blood pumps are deemed suitable for patients with different types of end-stage cardiac failure. Therefore, hemodynamic changes, such as heart rate, central venous pressure, cardiac index, systolic blood pressure, and pulmonary capillary wedge pressure, should be closely monitored after surgery, while the active administration of vasoactive drugs is necessary to ensure stable circulatory function. Thromboembolism and kidney failure are common complications that require extra attention. Anticoagulant therapy should be initiated early to prevent postoperative red blood cell damage, hemolysis, and thrombosis. All anticoagulants should be given by micro-pumps to ensure precise and even medication delivery, and the dosage should be adjusted accordingly based on the patient's adenosine triphosphate level and bleeding situation. Blood pump parameters should be closely monitored and recorded and then adjusted as needed, and emergency items should be available at all times in case of blood pump dysfunction.

Our country had a late start on vascular assist device research and has yet to report any successful clinical cases. This study is the first to systematically and comprehensively investigate the perioperative nursing management of axial-flow blood pump implantation in animals. Moreover, to meet the surgical requirement of artificial cardiac pump implantation in animals, we creatively designed and made a series of highly practical animal surgical instruments including a composite disassemblable bed for experimental animal transferring and monitoring, a multifunctional animal surgery bed, and portable medical supporting equipment. We have also applied for two national invention patents and one utility model patent. The information collected from this study provides a theoretical and practical foundation for the development and clinical application of domestically manufactured artificial cardiac pumps.

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Risk Factors, Clinical Features, Baseline Alanine Aminotransferase and CD4+ Count of Children with HIV Co-Infection with Hepatitis B and C at a Tertiary Hospital in Southwest Nigeria

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Abstract

Background: Human immunodeficiency virus and hepatitis B and C viruses are endemic in sub-Saharan African countries including Nigeria. Researchers have studied the burden of co-infection of HIV with hepatitis B and hepatitis C but the risk factors and clinical presentation have not been much addressed especially in children. Methodology: This was a prospective cross sectional study that determined the prevalence, risk factors, clinical features, baseline CD4+ count, CD4+ percentage, and alanine aminotransferase (ALT) of newly diagnosed, HAART naïve HIV co-infection among children who were managed at a Tertiary Hospital in Ilorin, Nigeria. Result: Of the 60 HIV-infected children recruited, 11.7% had HIV co-infection with HBV or HCV. Children with co-infections (mean age 8.43 ± 2.37 years) were significantly older than their HIV mono-infected counterparts (mean age 5.25 ± 3.96 years) (p = 0.011). There was no significant difference between HIV monoinfection and HIV co-infection with respect to gender (p = 0.758), ethnicity (p = 0.707), religion of parents (p = 0.436), family type (p = 0.184), social class (p = 0.535), previous transfusion (p = 0.053), scarification (p = 0.612), female genital mutilation (p = 0.778), and sharing of clippers (p = 0.806). The mean BMI, immunological staging (p = 0.535), baseline ALT (p = 0.940), and mean baseline CD4+ count (p = 0.928) were comparable. However, the body mass index of HIV co-infected children decreased with age up till age 10 years. Conclusion: There were no risk factors, nor clinical features predictive of co-infection identified in this study. Co-infection did not negatively impact baseline, CD4+ count and ALT.

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Keywords

Co-Infection, Hepatitis B, Hepatitis C, Human Immunodeficiency Virus, Acquired Immunodeficiency Syndrome, HIV, HBV, HCV, Alanine Aminotransferase, ALT, Highly Active Antiretroviral Therapy, HAART, Monoinfection, CD4+, Risk Factors for Co-Infection, Transmission, Hepatitis B Surface Antigen, HBVsAg

1. Introduction

The improvement in access to antiretroviral therapy (ART) has resulted in better survival of people living with HIV/AIDS and has made the obvious burden of chronic complications of HIV infection that manifestation may have been masked by high AIDS-related mortality in the pre-ART era [1]. The understanding of the shared routes of infection and risk factors of HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) has raised concern of the possibility and effects of co-infection with these viruses [2]-[4].

Hepatitis C virus infection has been found to accelerate the evolution and progression of liver disease in HIV-infected individuals [4]-[6]. There are also reports that HIV/HBV co-infected patients have higher levels of HBV replication, lower rates of spontaneous resolution of the HBV infection, a higher risk of reactivation of previous infections, and an increased risk of developing cirrhosis [5] [7] [8].

Co-infection of HIV with HCV and HBV is associated with increased toxicity of antiretroviral medications [5]. Other studies however report no impact of HBV co-infection on HIV disease progression [9]-[11].

Several studies have reported a significantly higher mean baseline ALT in co-infected patients than patients infected with HIV alone [12]-[14]. The mean $CD4^+$ cell counts in contrast are significantly lower among the HIV/HBV co-infected participants who also have slower rates of $CD4^+$ cell recovery compared with patients with HIV infection alone [8].

1.1. Risk Factors and Transmission of HIV, HBV and HCV

Vertical transmission also known as mother to child transmission accounts for almost all HIV infections in children younger than 13 years (greater than 90% of paediatric HIV infections in general), although the rate of vertical transmission has reduced significantly in region where there is adequate access to HIV care and support services [14] [15]. Other significant modes of transmission of HIV in children as shared with hepatitis B and C viruses include parenteral exposure to HIV infected blood and blood products, sexual contact with HIV infected persons (especially among adolescents and victims of sexual assaults), and intravenous drug use especially among adolescent boys, [15] believed to be less important in West African children than those in developed countries [14] [16].

The risk of vertical transmission of HBV which can occur in-utero, intrapartum, or postpartum, is up to 70% - 90% if the mother is hepatitis B envelope antigen (HBeAg) positive, compared to 0% - 30% if mother is HBeAg negative without immunoprophylaxis for the infant [17] [18]. Immunoprophylaxis using hepatitis B immunoglobulin administered soon after birth and HBV vaccination is highly protective, preventing chronic HBV infection in about 95% of infants whose mothers have HBV infection, but the coverage of universal HBV vaccination is very low in developing countries [19] [20]. Some researchers believe that vertical transmission is a less important mode of transmission of HBV in Africa children than their Asian counterparts partly due to lower prevalence of HBeAg in African pregnant women compared to those in Asia [10] [18]. Horizontal transmission of HBV occurs through unapparent blood or blood product exposures from parents, siblings, or playmates who are HBV infected leading to inoculation of HBV into cutaneous scratches, abrasions, or other lesions on mucosal surfaces [21]. Horizontal transmission is believed to be a predominant mode of transmission of HBV in regions endemic for HBV such as Africa, most infections occurring before five year of life [18]. The risk factors of HBV infection in childhood include: maternal HBV infection, transfusion of blood and blood products (largely eliminated where blood and blood products are routinely screened for HBV) [22] [23], use of unsterile instrument in traditional surgical practices (such as scarification, circumcision and female genital mutilation, uvulectomy), re-use of needles, contaminated house-hold articles (such as, tooth brush, razors, even toy) [19], known HBV infected family member, rape, and use of intravenous drug.

Hepatitis C virus shares similar routes of transmission and risk factors with both HBV and HIV [24] [25]. However, hepatitis C virus is more efficiently transmitted through direct contact with blood and blood products, thus, infection has been documented to be higher in recipients of contaminated blood and blood products. Sexual activity has been described as inefficient mode of transmission of HCV infection [4]. In childhood, vertical and perinatal transmission remains the most important means of infection with HCV, and has been reported to be enhanced by maternal HIV co-infection [4] [17].

In Benin, no association was found between risk factors such as circumcision, ear piercing, parenteral injections and blood transfusion with seropositivity for HBsAg or HCV [26]. This is similar to findings in Tanzania [27]. This lack of association of HIV/HBV or HCV co-infection with circumcision, ear piercing, parenteral injections support the believe that horizontal transmission during the first five years of life plays more significant role for HBV transmission in Sub-Saharan Africa than the use of contaminated instrument [4]. A study in Eastern Nigerian reported awareness and use of safety precautions such as use of new razor blade, earring, and surgical consumables by traditional healers that carry out scarification and ear piercing as possible factors that have reduced chances of contamination and transmission of infection through this means [28]. A study in China found high prevalence of HCV infection in HIV-infected children who acquire HIV infection through blood and blood products transfusion, and less HIV/HCV co-infection in children with vertically acquired HIV infection, supporting the role of blood transfusion in the transmission of HCV infection [3].

Intravenous drug abuse which is a high risk factor for the transmission of HCV is not a common risk behaviour identified in studies from sub-Saharan Africa [5] [13].

1.2. Effects of HIV Co-Infection with HBV and HCV

Publications have reported the adverse reciprocal interaction of HIV co-infection with HBV, HCV, or both HBV and HCV that affects every aspect of the co-infection, namely: viral replication, clinical presentation, response to therapy, and outcome of patients with the co-morbidities [12] [29]-[31]. Research has evaluated the effect of HIV infection on response to hepatitis B vaccination, and has documented reduced and less durable antibody titre after vaccination [4] [32]. Thus, fewer HIV infected children have protective antibodies against HBsAg after vaccination [33]. The rate of response to HB vaccination is directly proportional to CD4 counts, but has inverse relationship with HIV viral load, although there is no consensus on the immunological threshold at which vaccination becomes futile [4]. Co-infection of HIV with HBV has been reported to be associated with increased risk of chronic HBV infection, higher HBV DNA levels, thus, higher rates of cirrhosis, end stage liver disease, and death from liver diseases, especially in patients with low CD4 count [4].

It has been recommended that both anti-HBc and HBsAg should be used in screening for HBV infection in HIV/HBV co-infection because about 10% - 45% of patients with co-infection who have negative HBsAg tested positive for anti-HBc, and when evaluated further, have HBV DNA [4]. These patients are referred to as having occult HBV infection, and should be considered infected with HBV. Patients who have positive anti-HBc without HBV DNA should be regarded as having amnestic response and require no treatment [4] [34]. The goal of treatment in HIV co-infection with HBV is maximal suppression of hepatitis B viral replication evident by clearance of HBV DNA or hepatitis B e antigen (HBeAg), and improvement in liver disease [4]. Immune control is rarely achieved in patients with HIV/HBV co-infection [4].

The unfavourable effects of HIV/HCV co-infection has also been documented but the symptoms are milder and rate of progression of both hepatic and extrahepatic diseases appear to be slower in children. The natural history of HCV is accelerated, with an increase rate of progression to liver cirrhosis, decompensated liver disease, hepatocellular carcinoma, and death [35]. Extra-hepatic manifestations of HIV/HCV co-infection such as cognitive dysfunction and diabetes mellitus may negatively impact on the quality of life of patients with co-infection [4].

Hepatotoxic effects of antiretroviral drugs such as lamivudine and nevirapine, two commonly used first line antiretroviral drugs in developing countries are more likely to develop in HIV-infected children co-infected with HBV or HCV [29] [36].

Lamivudine is a drug frequently used in the treatment of chronic hepatitis B infection, but resistance to lamivudine is common in HIV/HBV co-infection, occurring in 90% of patients after 4 years of treatment with lamivudine [37]. This potentially, can lead to rapid development of lamivudine resistant HBV infection in resource limited settings, especially in sub-Saharan Africa where horizontal transmission of HBV is a significant mode of transmission.

Immune reconstitution inflammatory syndrome has been described in patients with HIV co-infection with HBV and HCV, associated with significant morbidity and mortality [38].

Few researches among children have tried to correlate the prevalence of HIV co-infection with HBV or HCV with baseline WHO clinical staging of HIV, because it is logical to expect advanced or severe HIV/AIDS in patients with co-infection [3] [9]. Two studies, one from Nigeria and China did not find significant difference in baseline WHO staging between HIV/HBV or HCV co-infection and HIV-monoinfection [3] [9]. These studies however, differ from the research findings in Cote d'Ivoire where children with HIV/HBV or HCV co-infections presented with Centre for Disease Control (CDC) HIV stage B or C disease compared with children who had HIV-monoinfection [39]. Among adults, a study in Nigeria has reported that the prevalence of HIV co-infection with HBV or HCV increases with HIV disease progression, similar to research finding in India [5] [25]. The finding of higher prevalence of HIV co-infection with HBV or HCV in patients with advanced HIV infection supports a rapid course of HIV disease progression in patients with co-infection.

Rawizza *et al.* [9] evaluated base line CD4 count, alanine aminotransferase (ALT), and WHO clinical stage of children with HIV infection and compared the results with children with HIV/HBV, HIV/HCV co-infection. They did not find significant difference in baseline CD4 count, WHO clinical stage, and ALT between HIV-monoinfection and HIV/HBV or HIV/HCV co-infections similar to a research finding in Cote d'Ivore [39]. Rawizza *et al.* [9] however found some HIV infected children who had significant ALT elevation to 5-fold the upper border of normal, this was however, not related to HBV or HCV co-infection [9]. The finding of normal ALT in HIV co-infection with viral hepatitis differs from a Tanzania study that found elevated ALT in children with HIV/HBV or HIV/HCV co-infections [27].

Rouet *et al.* [39] in Cote d'Ivoire evaluated the baseline HBeAg in children with HIV/HBV co-infection and followed these children for at least 18 months. It was found that 82% of children with HIV/HBV co-infection had chronic HBeAg positive HBV infection, with persistence of HBeAg beyond 18months in about 80% of these patients. Most of these patients had high level of HBV DNA titre, indicating that they were in the initial immunotolerant stage of HBV infection. It was pertinent to discover that only few of the these children with HIV/HBV co-infection had HBeAg seroconversion, and there was no significant difference at 18 months in terms of HBeAg seroconversion between HIV/HBV co-infected patients on HAART either containing 3TC or not and those without HAART, implying no remarkable benefit from HAART.

Few studies have addressed HIV co-infection with HBV or HCV among children globally, and especially in Nigeria [9]. Studies are required to address the magnitude, risk factors for co-infection and baseline immunological and liver function parameters in children with the co-morbidities. The risk of progression of HBV infection to chronicity in childhood, and the generally high rate of progression of acute HCV infection to chronicity, and their sequelae in adulthood makes determination of the burden of HIV co-infection with viral hepatitis B and C in childhood imperative. This study is a template for subsequent studies that will characterize the features and outcome of the co-infections.

1.3. Methodology

This was a prospective descriptive cross-sectional study of children age 2 months to 13 years who were HIV infected conducted in University of Ilorin Teaching Hospital (UITH), a tertiary institution located in Ilorin, in the North Central geopolitical zone of Nigeria. Recruitment of patients was carried out at the Paediatric Antiretroviral Therapy (ART) Clinic, Emergency Paediatric Unit (EPU), and Paediatric medical ward of the hospital. A total of 60 HIV-infected children were recruited into the study using the Andrew Fisher's formula to calculate the minimum sample size. The national seroprevalence of HIV used was 4.1%, and the tolerable margin of error was set at 0.05. Ethical clearance was obtained from the Ethical Review Committee of the hospital while individual informed consent was also obtained from the respective parent or care-giver of the child and written assent was also obtained from children aged 7 years and above before subject recruitment.

1.3.1. Subject Recruitment

This study was carried out over eleven month period, from January to October 2011. Consecutive patients who met the recruitment criteria were recruited into the study after informed consent. Recruitment of subjects was done by the investigator.

1.3.2. Inclusion Criteria

All antiretroviral drug naïve HIV infected children aged two months to 14 years whose parent gave consent, and children age 7 years to 10 years who gave assent to participate were recruited.

1.3.3. Exclusion Criteria

All HIV infected children on antiretroviral or antituberculous drugs were excluded from the study.

Potential eligible children whose parents did not give consent, or children 7 years to 14 years who did not give assent to participate in the study.

1.3.4. Data Collection

Semi structured questionnaire was used to obtain information on: socio-demographic characteristics, educational qualifications and occupations of parents, risk factors for transmission of HIV, HBV, and HCV, presenting symptoms of patients, anthropometric measurements, and laboratory parameters.

Socio-economic index scores were awarded to the occupations and educational attainments of parents or caregivers of subjects using the Oyedeji socio-economic classification scheme [40]. The anthropometry of each subject was taken and a detailed medical examination was conducted on each patient.

HBV infection was confirmed using Diaspot HBsAg (AZOG Inc. Phillipsburg, USA), a one step hepatitis B surface antigen test strip [41], while Hepatitis C infection was screened for using DiaSpot HCV, a one step hepatitis C virus test strip (AZOG Inc. Phillipsburg, USA) [42] [43]. Complete blood count, CD4 count, and Alanine aminotransferase assay were done for all patients recruited to the study by dedicated Laboratory scientists at the ART laboratory following standard laboratory procedure.

1.3.5. Data Analysis

Data was analyzed using Epi-info version 6 software. The results of investigation and other data collected on the proforma were entered into a master sheet using numerical codes. Frequency distribution tables and cross tabulation of variables were generated. Appropriate statistical tests were carried out as necessary. Level of significance was set at 0.05.

2. Results

General Characteristic of Study Population

Sixty HIV-infected children were recruited to the study, of which males were 31 (51.7%), and females were 29 (48.3%) giving a male female ratio of **1.1:1**.

Six patients (10%) tested positive for HBsAg, while only one (1.7%) of the subjects tested positive for HCV. The prevalence of HIV co-infection with HBV and HCV among this cohort was thus 11.7%. Among children with HIV co-infection, four (57.1%) were males while 42.9% of the co-infected patients were females, thus, HIV co-infection with HBV and HCV had no relationship with gender ($p = 0.925$). The mean age of HIV-monoinfected children was 5.25 ± 3.96 years, while children with HIV co-infection had a mean age of 8.43 ± 2.37 years (**Table 1**). Children with HIV co-infection were significantly older than HIV-monoinfected children (***t* = −3.034**, ***p* = 0.011**).

Table 2 summarizes the risk factors evaluated in this study. Among HIV-monoinfected children, 38 (72%) had HB vaccination, while only three (42.9%) of children with HIV co-infection with HBV and HCV had HB

Table 1. Age group distribution of children with HIV-monoinfection and HIV co-infection with HBV and HCV.

Age groups	HIV-monoinfection		HIV/HBV and HIV/HCV co-infections		x^2	*p*
	n (%)	Mean age	n (%)	Mean age		
2- < 18 months	4 (100.0)	11.0 ± 4.1	0 (0.0)	0.0	-	-
18- < 60 months	20 (95.2)	37.0 ± 11.3 months	1 (4.8)	48.0 months	0.641	0.432
5- < 10 years	24 (88.9)	6.5 ± 1.4 years	3 (11.1)	8.0 ± 1.0 years	0.389	0.777
10 - 13 years	5 (62.5)	11.2 ± 1.3 years	3 (37.5)	10.3 ± 0.6 years	0.032	0.064

Table 2. Risk factors for HIV co-infection with HBV or HCV.

Risk factors	HIV-monoinfection		HIV co-infection		x^2	*p*
	n = 53	%	n = 7	%		
HB vaccination	38	71.7	3	42.9	0.134	0.268*
Sexual activity	1	1.9	0	0.0	-	-
Circumcision	23	43.4	4	57.1	0.389	0.777*
Family History of HBV	1	1.9	0	0.0	-	-
Previous surgery	4	7.5	0	0.0	-	-
Blood transfusion	9	17.3	4	57.1	3.748	0.053*
Scarification marks	8	15.1	1	14.3	0.306	0.612*
Sharing clippers	16	30.2	3	42.9	0.403	0.807*
Sharing needles	1	1.9	0	0.0	-	-
Tattooing	4	7.5	0	0.0	-	-

*Yate corrected chi.

vaccination. However, there was no significant difference with respect to HB vaccination ($x^2 = 0.134$, $p = 0.268$). Approximately fifty seven percent (4 out of 7) of HIV co-infected children had been transfused with blood, while 17% (9 out of 53) of HIV-monoinfected children had history of blood transfusion. There was no statistically significant difference between HIV monoinfection and co-infection with respect to previous blood transfusion ($x^2 = 3.748$, $p = 0.053$). There was no significant difference between HIV-monoinfected children and those with HIV co-infection in terms of: scarification ($x^2 = 0.306$, $p = 0.612$), circumcision or female genital mutilation ($x^2 = 0.389$, $p = 0.777$), and sharing of clippers ($x^2 = 0.403$, $p = 0.807$). Risk factors such as previous surgery, traditional uvulectomy, sexual activity, tattooing, parenteral use of illicit drug, and known family history of hepatitis were not common in this cohort.

Common physical examination findings in the study population included: scarification marks, weight loss, generalized lymphadenopathy, Painless parotid enlargement and hepatomegaly (**Table 3**). However, when HIV-monoinfected children were compared with those with HIV/HBV and HIV/HCV co-infections, there was no significant difference with respect to physical examination finding of scarification marks ($x^2 = 0.103$, $p = 0.206$), weight loss ($x^2 = 0.247$, $p = 0.499$), microcephaly ($x^2 = 0.211$, $p = 0.421$), generalised lymphadenopathy ($p = 0.692$), abdominal distension ($p = 0.608$), and hepatomegaly ($x^2 = 0.411$, $p = 0.822$). Other physical examination finding whose frequencies were not sufficient for statistical analysis included: pallor, jaundice, painless parotid enlargement, skin rash, ear discharge, lung crepitations, ascites, splenomegaly, and ophthalmopathy.

The mean BMI of the study population was 14.21 ± 2.54Kg/m^2. Children with HIV monoinfection had a mean BMI of 14.17 ± 2.65 Kg/m^{2}while children with HIV co-infection with HBV and HCV had a mean BMI of 14.56 ± 2.65 Kg/m^2. There was no significant difference in mean BMI between children with HIV monoinfection and those with co-infection ($p = 0.711$). However, **Figure 1** shows that the BMI of children with co-infection shows that the BMI of patients with HIV co-infection with HBV and HCV decreased as age advanced up till the age of 10year with a significant negative correlation between ages and BMI ($r = -0.83$, df = 5, $\alpha = 0.05$). There was no significant correlation between the ages and BMI of the HIV-monoinfected children ($r = -0.1313$, df = 51, $\alpha = 0.05$) (**Figure 2**).

The mean baseline CD4$^+$ counts of HIV-monoinfected children older than 59 months was not significantly different from that of HIV/HBV and HIV/HCV co-infected children of the same age group ($t = 1.022$, $p = 0.314$) (**Table 4**). Among children younger than five years, there was only one child with HIV/HBV co-infection and the group was not subjected to further statistical analysis.

3. Discussion

This study evaluated the prevalence, risk factors and physical examination findings of children with HIV co-infection with HBV and HCV. The prevalence of HIV co-infection in this study was 11.7%. The prevalence had earlier been reported [44].

Table 3. Clinical features of HIV-monoinfection and HIV/HBV or HCV co-infection.

Clinical features	HIV-monoinfection n = 53 n (%)	HIV co-infection n = 7 n (%)	x^2	*p*
Weight Loss	19 (36.5)	4 (57.1)	0.247	0.499*
Fever	3 (5.7)	0 (0.0)	-	-
Scarification	8 (15.1)	3 (42.9)	0.103	0.206*
Jaundice	0 (0.0)	0 (0.0)	-	-
Pallor	4 (7.5)	0 (0.0)	-	-
Abdominal distension	7 (13.2)	1 (14.3)	0.304	0.608*
Tenderness	0 (0.0)	0 (0.0)	-	-
Ascites	0 (0.0)	0 (0.0)	-	-
Splenomegaly	3 (5.7.0)	0 (0.0)	-	-
Hepatomegaly	9 (17.0)	2 (28.6)	0.411	0.822*
Microcephaly	28 (53.0)	2 (28.6)	0.211	0.421*
Painless parotid enlargement	2 (4.0)	0 (0.0)	-	-
Generalised lymphadenopathy	6 (11.3)	1 (14.3)	0.346	0.692*
Rash	4 (7.6)	0 (0.0)	-	-
Pulmonary crepitations	3 (5.7)	0 (0.0)	-	-
Ear discharge	1(1.9)	0 (0.0)	-	-
Opthalmopathy	0 (0.0)	1 (14.3)	--	-

*Yate corrected chi

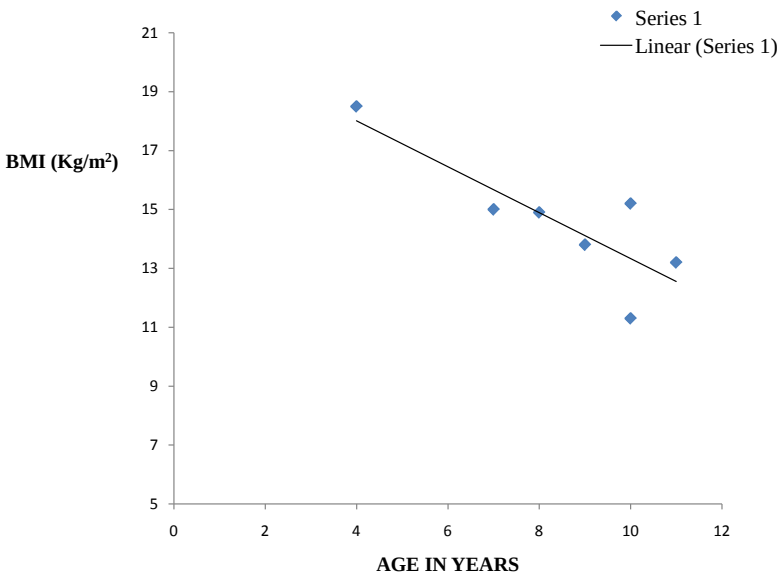

Figure 1. Relationship between BMI and age of HIV co-infected children.

The history of previous blood transfusion was found in 67% of co-infected children in contrast to only 17% of HIV-monoinfected children, however, this difference was not statistically significant.

Risk factors such as circumcision or female genital mutilation, scarification, tattooing, sharing of clippers, had no significant association with HIV/HBV or HIV/HCV co-infections, similar to results of other studies in Nigeria and Africa [26] [27].

Some risk factors such as traditional uvulectomy, sexual activities, and illicit drug injection were rare in this

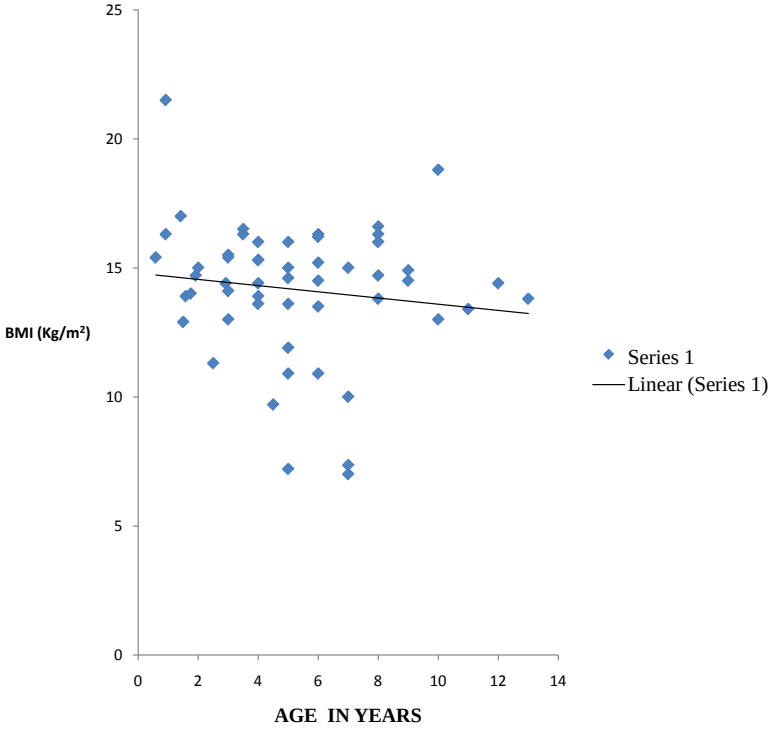

Figure 2. Relationship between BMI and age of HIV-monoinfected children.

Table 4. Mean $CD4^+$ count and $CD4^+$ percentages.

	HIV-monoinfection			HIV co-infection			*t*	*p*
Age groups	n = 53	Mean $CD4^+$ count (cells/L)	Mean $CD4^+$ %	n=7	Mean $CD4^+$ count (cells/L)	Mean $CD4^+$ %		
<11 months	3	1004 ± 887	29.0 ± 19.9	0	0	0.0	-	-
12 - 35 months	8	1811 ± 1536	23.9 ± 7.3		0	0.0	-	-
36 - 59 months	13	823 ± 576	22.8 ± 11.4	1	336	10.0	-	-
≥5 years	29	745 ± 657		6	442 ± 684		1.022	0.314

cohort. Social stigma associated with risk factors such as sexual activities in our society may make people deny this history. Improvement in heath, and reduction in risky traditional surgical practices may partly explain the low prevalence of risk factors such as genital mutilation, and traditional uvulectomy [26].

There was only one suspected case of sexual transmission in a sexually active adolescent girl who was living with her maternal grandmother that was a commercial sex worker.

There was no case of known family history of hepatitis B or C in this study. History of hepatitis B in family members living together is a risk factor for horizontal transmission of HBV. However, this information was based on informant's knowledge and not medical records of parents or family members, and may thus be a reflection of low level of awareness of HBV and HCV infection in the community. Community awareness of hepatitis B or C infection, and the basic knowledge of mode of spread of these viruses have been known to correlate with the prevalence of hepatitis B or C in the community, being relatively lower in communities with high level of awareness and higher in those with low level of awareness [45].

There was no significant difference between the presenting physical examination findings of HIV-monoinfected and HIV/HBV or HIV/HCV co-infected children in this cohort. This suggests that co-infection did not negatively affect the clinical presentation of both HBV and HCV infection in this cohort. The few paediatric

studies that have evaluated the clinical presentation of children with HIV co-infection with HBV or HCV used the WHO clinical staging, and found no significant difference between children with HIV monoinfection and those with HIV co-infection with HBV or HCV with respect to WHO clinical staging. [3] [9] However, a study in Cote de Ivoire reported that children with HIV co-infection with HBV or HCV presented with Center for Disease Control and Prevention clinical stages B and C compared to stage N or A in the HIV-monoinfected group [39]. Chronic hepatitis B and C viruses in childhood usually run indolent courses until chronic liver diseases manifest, most often in adulthood [46]. This finding of no significant impart of co-infection on presenting symptoms of HIV infection or viral hepatitis B or C infection supports a benign course of HBV and HCV disease in childhood.

The progressive fall in the body mass index of HIV co-infected children as their ages advanced as seen in this study was not observed in the HIV-monoinfected counterparts. This might suggest recent onset of progressive fall in weight relative to height in patients with co-infection. Although, this relationship between BMI and age of children with HIV co-infection with HBV and HCV has not been reported, progressive fall in BMI may be an early sign of HIV co-infection with HBV and HCV.

This study also shows that both HIV-monoinfected and HIV-coinfected children had comparable levels of immunodeficiency, similar to the findings by Telatela *et al.* in Tanzania [27]. This further confirmed that co-infection may not significantly accelerate HIV disease progression in childhood. Other studies in Nigerian children also did not find significant differences in the baseline immunological parameter between HIV co-infection and HIV monoinfection [9] [26].

The mean baseline alanine aminotransferase of the two groups of children were comparable. Similar finding had been reported by Rawizza *et al.* [9] in Nigeria, but differs from the findings of the work in Tanzania [27] that found a four-fold risk of ALT elevation in HIV/HBV or HIV/HCV co-infected children compared with HIV-monoinfection. However, the study population in Tanzania is relatively older, and some of the patients were using antiretroviral drugs most of which are potentially hepatotoxic such as nevirapine and efavirenz [47].

Approximately 9% of HIV-monoinfected children in this study had elevated serum ALT ranging from 1.1 to 2 times the upper limit of reference values. All these five patients were aged 10 years and above, having serum ALT that is directly related to their ages. This supports the fact that advancing ages have correlation with clinical severity. Such elevation of ALT had been reported earlier in Nigeria, and such patients probably have early hepatic manifestation of HIV and should be monitored to identify the evolution and course of HIV infection in them [9].

4. Conclusion

There was no significant association of risk factors such as blood transfusion, traditional uvulectomy, scarification and tattooing with co-infection in this study. There was no clinical feature predictive of HIV co-infection with HBV and HCV in this cohort. Hepatitis B virus or HCV co-infection did not negatively impact on baseline immunological parameters of HIV infected children. There was no difference between HIV-monoinfected and co-infected children with respect to baseline ALT. The baseline $CD4^+$ count and percentages of HIV-monoinfected children and HIV infected children with HBV and HCV were similar. There was a need for longitudinal studies that would characterize the evolution and course of HIV-infected children with HBV or HCV co-infection.

5. Limitations

Screening for HBV co-infection in this study was by the use of HBsAg alone, which does not necessarily indicate current infection.

Secondly, HCV infection was not confirmed by plasma PCR for HCV-RNA, making it impossible to distinguish active HCV infection from spontaneously cleared infection.

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