دبي الصحية
DUBAI HEALTH

**Mohammed Bin Rashid University of Medicine and Health Sciences**

**College of Medicine**

# EVALUATING THE POTENTIAL OF VIRTUAL REALITY INTERVENTION IN ALLEVIATING PAIN AND ANXIETY AMONG THALASSEMIA PATIENTS DURING INTRAVENOUS CANNULATION: AN INTERVENTIONAL CROSS-OVER STUDY, 2023-2024

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**This research proposal is submitted in partial fulfilment of the requirements for the Research Methods 2 Course (MEDC2424) as part of the Bachelor of Medicine, Bachelor of Surgery (MBBS) Programme**

**Under the Supervision of Dr. Yacine Hadjiat (MBRU)**

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## Declaration of Original Work

We, Sameer Khan, Humza Rathore, Fawaz Mohammed, the undersigned, undergraduate medical students at the Mohammed Bin Rashid University of Medicine and Health Sciences (MBRU), and the authors of this research proposal titled "*Evaluating the Potential of Virtual Reality In Alleviating Pain and Anxiety among Thalassemia Patients During Intravenous Cannulation: An Interventional Cross-Over Study, 2023-2024",* hereby, solemnly declare that this research proposal is our own original research work that has been conducted and prepared by us under the supervision of Dr. Yacine Hadjiat (MBRU). This work has not previously been presented or published, or formed the basis for the award of any academic degree, diploma or a similar title at this or any other university. Any materials borrowed from other sources (whether published or unpublished) and relied upon or included in this research proposal have been properly cited and acknowledged in accordance with appropriate academic conventions. We further declare that there is no potential conflict of interest with respect to the proposed research outlined in this research proposal.

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**Study Synopsis** (suggested ≤150 words)

Virtual reality's immersive and distraction-based nature has the potential to offer relief to thalassemia patients undergoing blood transfusions and experiencing pain. VR has demonstrated effectiveness in reducing pain and anxiety in other patient populations, making it a valuable intervention to explore within the thalassemia context.

We propose to conduct an interventional cross-over study with a cohort of around 100 patients, where initial data is collected without VR for measuring baseline, then VR is implemented twice in a 3-week interval between sessions. We will investigate the impact of VR software on patients' pain and anxiety during the intravenous cannulation procedure, compared with a standard care program. Our primary outcomes involve assessing patient pain and anxiety, while secondary outcomes are fatigue, boredom, and overall patient satisfaction.

Pain and anxiety will be measured both subjectively (VAS) and objectively (cardiac frequency) as secondary exploratory measures. We will also look to assess healthcare providers' and family members' satisfaction levels pre and post VR intervention. The aim of this study is to evaluate the benefits of VR programs in reducing patients' pain and anxiety.

## Introduction

*Background and Rationale:*

Hemoglobinopathies, specifically β-thalassemia, are a significant health concern in the UAE, affecting 8.5% of the population [1,2]. These genetic disorders often require frequent blood draws, chelation therapy, and transfusions, causing stress and impacting quality of life for patients [3].

Repeated pain in children with chronic diseases such as thalassemia can cause behavioural changes in their adolescence, such as anxiety, social problems, and decreased attention. This condition can further impact the quality of life of thalassaemic children as adults [4]. Therefore, nurses must provide specific interventions to improve the child's comfort during invasive procedures.

Virtual reality (VR) is a technology that enables patients to be projected, via a computer system, into an immersive 3-dimensional virtual world. This specificity gives VR a highly immersive and distracting capacity. VR effectively diverts the patient's attention away from the source of pain, thereby diminishing his or her conscious perception of it [5,6].

In recent years, the number of studies investigating the use of Virtual Reality (VR) as a non-pharmacological method of reducing anxiety and pain has grown rapidly. Numerous studies have confirmed this analgesic effect of VR on different modalities such as invasive procedures in chronic diseases such as thalassemia [4,7]. These benefits apply to a multitude of interventions in order to improve the management of pain and/or anxiety, such as wound care [8,9], needle insertion in children [10,11], perioperative management [12,13] and chronic pain relief [14].

Therefore, we propose to conduct an interventional cross-over study to investigate the impact of VR software on patients' pain and anxiety during the intravenous cannulation procedure, compared with a standard care program. The aim of this study is to evaluate the benefits of VR programs in reducing patients' pain and anxiety.

*Study Aim:*

The primary aim of this study is to assess whether VR has a greater therapeutic impact on patient anxiety and pain perception compared to the standard of care during intravenous cannulation

procedures among thalassemia patients. This study will allow us to conclude on the effectiveness of virtual reality as an adjuvant medical device during the intravenous cannulation procedure.

*Study Objectives:*

- Evaluate the impact of VR-induced 3D immersion on pain and anxiety during cannulations through visualization of Healthy Mind VR therapeutic sessions.

- Comparison of patients' anxiety levels before and after the procedure with and without VR.

- Comparison of patients' pain levels before and after the procedure with and without VR.

*Research Hypothesis:*
There will be an improvement in the pain and anxiety measurement parameters with the use of virtual reality during the intravenous catheterisation procedure in thalassemia patients.

**Methods**:

This is an interventional cross-over, single-center study comparing virtual reality and standard care during intravenous cannulation for thalassemia patients at the Thalassemia Center in Dubai. The study is planned between April 2024 and June 2024.

Participants:
Inclusion criteria:

- Patient with diagnosis of thalassemia
- Thalassemia patient undergoing cannulation intravenous procedure
- Patients aged above >7 years (male, female, adults, paediatric, national and non-national) admitted at the referral center of thalassemia in Dubai

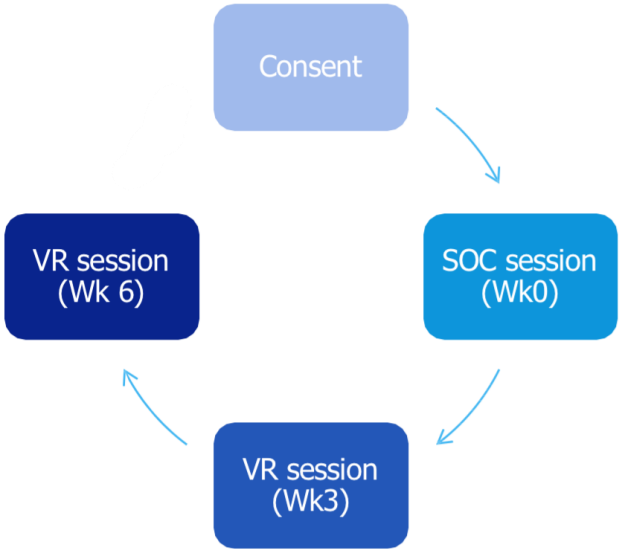
Exclusion criteria:

- Pregnant or nursing woman
- Patient of legal age but subject to legal protection measure or unable to express their consent
- Patient suffering from uncontrolled epilepsy
- Patient with visual or auditory disorders
- Patient suffering from claustrophobia or motion sickness
- Patient with face infection
- Patient with dissociative psychiatric pathologies and autism

After consulting the patients' medical records, and checking that there are no exclusion criteria, the investigators will introduce themselves to the patients and their families, informing them that they are eligible and offering them to take part in the study.
Patients will be informed that the study aims to investigate the immersive effect of VR during intravenous cannulation procedure, and they will be provided with a patient information sheet and flyer.
If the patient agrees in principle to take part in the study, and after obtaining informed, signed, written consent, each patient will be given a personalized schedule of the various management appointments and the questionnaires used as part of the protocol.

Interventions:

Patients will benefit from the standard of care for their first visit, then they will have a VR session on their second visit, then another session in VR for their third visit. The VR session starts 5 minutes before the intravenous cannulation procedure, 10 minutes during the procedure and 5 minutes after, for a total of 20 minutes. Before and after the intravenous cannulation procedure, the investigator will complete the Case Report Form for data collection from patients.
All participants will complete questionnaires before and after the procedure at visit 1 (V1), V2 and V3. The interval between visits is 3 weeks, in line with clinical practice at the referral centre.




The two options for managing anxiety and general symptoms are:

**1) Standards of care (SOC) :**

Thalassemia patients require lifelong monthly blood transfusions to survive. During routine visits, an experienced healthcare provider inserts intravenous cannulation under aseptic technique. Children are escorted by parents to offer support and distraction. This short procedure is accompanied by pain and anxiety for all the involved parties.

**2) Virtual reality (VR)**

HEALTHY MIND© VR (Paris, France): a 15-minute VR therapeutic session immersing the patient in an artificial world created from computer-generated images using software connected to the PICO 4E headset. The patient can choose one of several types of environments (beach, mountains, lake and others) using synthetic animated images, breathing exercises and advanced psychological/relaxation principles such as cardiac coherence or hypnotic verbal accompaniment.

Variables will be reported in a standardized way in the CRF in the following order:

- Before intravenous cannulation
    - Patient identification number
    - Patient demographics (gender and age)
    - Inclusion and exclusion criteria
    - Patient's VAS for pain intensity
    - Patient's VAS for anxiety
    - Patient's VAS for fatigue
    - Patient's VAS for cramps and heart rate measurement

- After intravenous cannulation:
    - Characteristics of intravenous cannulation. Specificity.
    - Patient's VAS for pain intensity
    - Patient's VAS for anxiety
    - Patient's VAS for fatigue
    - Patient's VAS for cramps and heart rate measurement
    - Patient's VAS for comfort and acceptability of VR headset use

**Data collection**

| | Pre inclusion V0 (*) | Visite 1 | | Visite 2 | | Visite 3 | |
|---|---|---|---|---|---|---|---|
| | | Before | Post | Before | Post | Before | Post |
| Screenning and information | ✓ | | | | | | |
| Consent form signed | ✓ | | | | | | |
| Demographic Data [1] | | ✓ | | | | | |
| Physiological data [2] | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| VAS[3] Anxiety, Pain and Fatigue | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| HAD scale | | ✓ | | | ✓ | | ✓ |
| Patient/Family Satisfaction | | | ✓ | | ✓ | | |
| | | | | | | | |
| Professional Satisfaction | | | | | | ✓ | |

**Expected Outcomes**

Primary outcomes: Evaluated by the Visual Analogue Scale (VAS)

- Evaluate the impact of VR-induced 3D immersion on anxiety during cannulations through visualization of Healthy Mind VR therapeutic sessions (using a PICO 4E VR headset). Comparison of patients' anxiety levels before and after the procedure with and without VR. Assessed by visual analog scale (VAS).

- Evaluate the impact of VR-induced 3D immersion pain during cannulations through visualization of Healthy Mind VR therapeutic sessions (using a PICO 4E VR headset). Comparison of patients' pain levels before and after the procedure with and without VR.

Secondary outcomes: Evaluated by the Visual Analogue Scale (VAS)

- Evaluation of fatigue levels after the procedure for patients with and without VR.

- Examine factors associated with boredom and weariness with and without VR.
- Evaluation of patient satisfaction with and without VR.
- Assessment of healthcare professionals' satisfaction levels during and after the procedure with and without VR.
- Assessment of family members' satisfaction levels during and after the procedure with and without VR.

- Assessment of other outcomes of interest (exploratory)
    - Evaluation of the heart rate with and without VR (cardiac frequency)

**Sample size calculation:**

Due to the exploratory nature of the study, the sample size was calculated on the basis of the number of possible orders of relaxation sessions, which was calculated as follows: 3 types of options x 3 x 2 = 18 possible session orders.

At least two different patients had to be enrolled for each type of option (i.e. 36 patients), to ensure a homogeneous distribution of the different possible orders of relaxation within the study population. 100 patients had to be enrolled in the study, to take account of patients lost to follow-up and missing data. Study power was set at 80% to demonstrate a clinically significant difference greater than 2, with an alpha threshold of 0.05.

Statistical analysis of primary objectives:

The difference between two sessions (VR vs SOC) will be followed by a comparison of the proportions of patients who achieved at least a 25% improvement in anxiety, pain, fatigue, and depression, assessed by the VAS and HAD scale in post-cannulation procedure. The value provided to patients in the VR session during intravenous cannulation procedure and patients with SOC, will be compared using Student's t-test, after verification of the homoscedasticity hypothesis by a Levene's test.

If this hypothesis is not verified, the Mann-Whitney test will be performed, for which the number of patients required to maintain 90% power is 35 per group. If the reduction is not 25% but only 20%, with a power of 80%, this difference will be highlighted.

A 2-factor repeated-measures ANOVA model (VR vs. non-VR session and time before vs. time after) will be developed. Another statistical model will be developed, in order to see the time and session effect and to see if there is an interaction between the 2 factors. Finally, the correlation between basal anxiety scores on the different VAS, HAD scales will be estimated using Pearson's or Spearman's coefficients; the same statistical approach will be used to assess correlations between basal anxiety and their levels measured after the cycles by the VAS.

Statistical analysis of secondary objectives:

The difference between two sessions (VR vs SOC) will be followed by a comparison of the proportions of patients who achieved at least a 25% improvement in satisfaction, assessed by the VAS. Comparison will be carried out using the same method used for primary objectives.

Risk factors associated with dissatisfaction will be explored using uni and multivariate logistic regression models.

**Overall ethical considerations**

This study is useful both for its scientific contribution and for improving the comfort of thalassemia patients undergoing invasive procedures such as intravenous cannulation. Through this study, we will gain insight into the impact of virtual reality as an adjuvant to care for intravenous cannulations.

Our research will be conducted in accordance with the Declaration of Helsinki and the National Act on Research Involving Human Subjects. We will ensure that no coercion or pressure to participate is exerted on patient-participants. Written informed consent will be obtained from each participant. At any time and without explanation, participants may leave the study without any effect on future care, treatment or working conditions.

With the exception of necessary personal data (socio-demographic information), members of the research team will maintain confidentiality with patient information. Participant data will be anonymised or coded as appropriate and stored securely.

**Limitations**

A limitation of our study is that randomising the order of intervention sessions was not favourable for our investigation. Because our participants all suffer from chronic disease, the most appropriate way to get a baseline for pain and anxiety perception is before exposure to VR intervention. If done in an alternative manner, i.e. starting with a VR session and then not having VR, it would be more likely for patients to over-report their feelings of pain or anxiety, thus skewing the results. Hence, ordering the sessions in the way that was ultimately decided was, we believe, in favour of reducing bias.

The results of this study will be applicable to all population groups which do not fall under our exclusion criteria (as mentioned in the methods).

**Project Timeline**

| | Feb 2024 | Mar 2024 | 15th April – 15th June | July 2024 | Aug 2024 | Nov-Dec 2024 |
|---|---|---|---|---|---|---|
| **IRB Submission** | | | | | | |
| **Site preparation, staff training** | | | | | | |
| **Screening and inclusion** | | | | | | |
| **Data management** | | | | | | |
| **Statistical analysis** | | | | | | |
| **Dissertation writing** | | | | | | |

**Acknowledgements**

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**Appendix**