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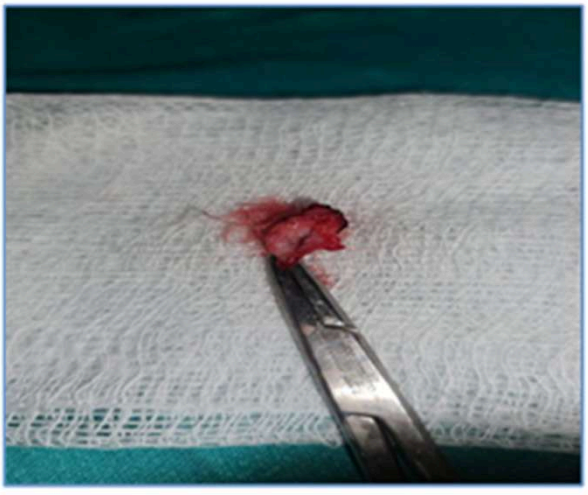
N B E J M S

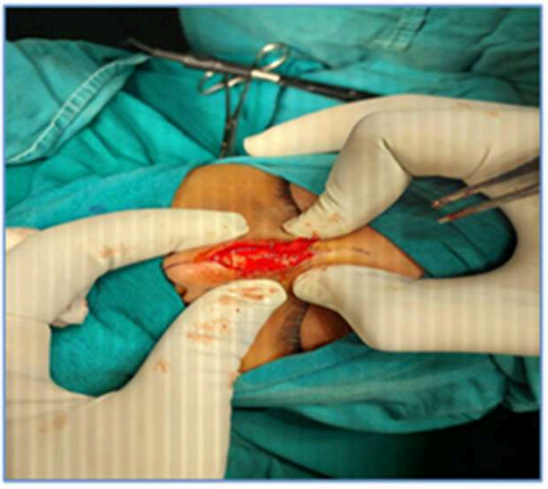
Measuring the hernia defect (Length)

Incision made upto peritoneum

Epithelial lined sinus tract with a tuft of hair



Intra operative image of nasal dorsum



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EDITORIAL

Redefining Pediatric Surgical Oncology: Gene Therapy, Nanorobots & Theranostics

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Pediatric surgical oncology stands at the threshold of a technological revolution. The high burden of childhood cancer has made it an urgent priority for biomedical innovation. In the field of pediatric surgical oncology, the high prevalence of cancer in children makes their treatment a key priority for scientific research. Emerging approaches are offering new hope in improving outcomes for these young patients.

Among the most promising advancements are gene therapy, nanorobotics & theranostics, which are transforming our approach to detection, diagnosis, and treatment.

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Gene therapy is emerging as a powerful tool in the fight against childhood cancer. One notable breakthrough involves targeting glycosylation pathways closely linked to tumor progression. The MGAT5 gene, for instance, encodes an enzyme responsible for modifying carbohydrate chains that fuel tumor growth. Knockout strategies targeting MGAT5 are now being explored as viable therapeutic interventions. An example of the MGAT5 gene's involvement in pediatric surgical tumors is seen in neuroblastoma, a common extracranial solid tumor in children.

Neuroblastoma and MGAT5

In neuroblastoma, overexpression of the MGAT5 gene has been associated with increased tumor aggressiveness and poor prognosis. MGAT5 encodes a glycosyltransferase that enhances the branching of N-glycans on cell surface glycoproteins. These branched glycans facilitate:

- Enhanced tumor cell adhesion,
- Increased motility and invasiveness, and
- Immune evasion, by modulating how cancer cells interact with the surrounding environment.

By knocking out or silencing MGAT5, researchers have observed reduced tumor cell proliferation and metastasis in preclinical models, making it a promising therapeutic target in pediatric neuroblastoma.

As our understanding of the genome advances, such interventions will become increasingly personalized.

☐ Non-invasive diagnostics—Equally significant is the role of non-invasive diagnostics. Mutations in mitochondrial DNA—detectable from something as simple as saliva samples—are being linked to specific pediatric tumors. This opens new pathways for early screening and prevention, reducing the need for invasive biopsies and increasing diagnostic speed and accuracy.

A strong example of the role of non-invasive diagnostics using mitochondrial DNA (mtDNA) in pediatric tumors is found in medulloblastoma, the most common malignant brain tumor in children.

Medulloblastoma and Saliva-Based mtDNA Mutation Detection

Researchers have identified specific mitochondrial DNA mutations associated with medulloblastoma, particularly in oxidative phosphorylation (OXPHOS) genes, such as *MT-ND1* and *MT-CO1*. These mutations can alter energy metabolism in tumor cells and have been linked to tumor subtypes and prognosis.

Importantly, such mtDNA mutations have been detected in saliva-derived epithelial cells, enabling:

- Early, non-invasive detection,
- Molecular subtyping of tumors (which guides treatment), and
- Monitoring of recurrence or minimal residual disease over time without repeated invasive procedures.

This saliva-based approach holds promise for use in children, where traditional biopsies or repeated MRIs are either risky or logistically challenging.

☐ Therapeutics—Nanorobots equipped with biosensors advancing drug delivery and surgical precision in pediatric oncology:

1. **Neuroblastoma: Dual-Mode Nanoparticles for Imaging and Therapy**

Dual-mode nanoparticle probes combine magnetic resonance imaging (MRI) and fluorescence imaging to enhance tumor visualization in neuroblastoma. These nanoparticles target neuroblastoma cells, enabling precise imaging and potential therapeutic applications.

2. **Neuroblastoma: NIR-II Nanoprobes for Tumor Differentiation**

Matrix metalloproteinase 14 (MMP14)-activatable NIR-II nanoprobe has been designed to distinguish neuroblastoma tumor tissues from surrounding non-cancerous tissue. This nanoprobe emits fluorescence upon activation by MMP14,

which is overexpressed in neuroblastoma cells, aiding in precise tumor localization.

3. Theranostics

Theranostic agents are molecules or nanostructures designed to combine both diagnostic imaging and therapeutic treatment into a single entity. This approach allows for real-time monitoring of disease progression and treatment response, enabling more personalized and effective therapies.

Tumor-targeting theranostic agents are innovative, dual-function molecules or nanoparticles designed to both diagnose and treat cancer by specifically targeting tumor cells. They combine imaging capabilities with therapeutic agents, allowing for accurate tumor detection and treatment. This approach offers advantages over traditional therapies, including improved targeting, reduced toxicity, and enhanced efficacy. For example, use of radioisotopes to first image a patient's tumor for diagnostics and then therapeutically treat that tumor.

Neuroblastoma: Gene-Loaded Nanoparticles for Targeted Therapy

Ligand-modified, gene-loaded nanoparticles can serve as tumor-targeting theranostic agents. These nanoparticles are engineered to deliver therapeutic genes specifically to neuroblastoma cells while allowing optical imaging to monitor treatment efficacy.

☐ Chemotherapy toxicity- it remains a major concern in pediatric patients.

Nanorobots, equipped with biosensors, are redefining drug delivery and surgical precision. These devices use nanowire-based sensors to detect subtle biochemical changes, such as early markers of metastasis, enabling clinicians to act sooner and with greater confidence.

Perhaps most striking is the use of quantum dots—fluorescent nanoparticles that bind to tumor cells. Once tagged, these cells become visible under surgical imaging, allowing for more accurate tumor resection. Conjugating tumor-specific ligands to these nanocrystals transforms them into highly specific surgical beacons. Beyond detection, intelligent nanorobots can also navigate vascular networks, identify tumors, and deliver drugs directly to the disease site, minimizing systemic exposure and maximizing therapeutic effect.

Following are some examples where nanorobots equipped with biosensors are emerging to enhance drug delivery and surgical precision:

1. **Targeted Drug Delivery in Pediatric Neuroblastoma**

Nanorobots can be functionalized with tumor-targeting ligands (e.g., antibodies against GD2, a surface antigen overexpressed in neuroblastoma).

- These devices **navigate the bloodstream**, bind specifically to neuroblastoma cells, and **release chemotherapy drugs** locally, minimizing systemic toxicity.
- Biosensors detect **tumor-specific pH or enzymatic activity** to trigger drug release at the tumor site.

2. **Fluorescent Quantum Dots for Intraoperative Guidance in Wilms Tumor**

In Wilms tumor (nephroblastoma), fluorescent quantum dot-labeled nanoparticles tag tumor margins.

- During surgery, these labeled cells emit light under specific wavelengths, allowing surgeons to visually distinguish tumor tissue from healthy kidney tissue in real time.
- Biosensors in the nanorobots can detect biochemical signals (e.g., hypoxia or lactate) to further refine localization.

3. Smart Nanorobots for Medulloblastoma Monitoring

For pediatric brain tumors like medulloblastoma, nanorobots may be introduced into cerebrospinal fluid (CSF) to detect early biochemical markers of recurrence using biosensors (e.g., glioma-associated miRNA or protein fragments).

- These sensors transmit signals externally, offering real-time monitoring without repeated MRIs or lumbar punctures.

4. Multifunctional Gold Nanoparticles in Osteosarcoma

In osteosarcoma, gold-based nanorobots can serve both therapeutic and diagnostic (theranostic) roles.

- They carry doxorubicin or cisplatin, release it in response to tumor-specific cues (e.g., acidic pH), and simultaneously emit imaging signals detectable during surgery.
- Some platforms include magnetic targeting to direct the nanorobots to tumor locations preoperatively.

These technologies are still largely experimental or in early clinical research, but they are rapidly progressing and may soon become integral in pediatric surgical oncology.

Together, these advances suggest a future where pediatric cancer care is not only more precise and effective, but also far less invasive and traumatic for young patients. The integration of gene-editing tools, biosensor technologies, and surgical nanodevices represents more than innovation—it represents a paradigm shift.

In the race against pediatric cancer, these tools are not just helpful—they are essential.

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ORIGINAL ARTICLE

Pre-Operative Intravenous Iron Therapy in Patients Undergoing Coronary Artery Bypass Surgery on Cardiopulmonary Bypass: A Non-Randomized Study

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Abstract

Objective: To study if preoperative iron and vitamin B_{12} supplementation in anaemic patients undergoing coronary artery bypass graft (CABG) surgery would reduce transfusion requirements perioperatively. **Materials and methods:** In this prospective non-randomised study, consenting patients received 20 mg/kg of ferric carboxymaltose intravenously and 1-mg of vitamin B_{12} subcutaneously (treatment arm). The control arm did not receive supplements. The primary outcome was perioperative transfusion requirement. Secondary outcomes included duration of ventilation and intensive care stay. The difference in transfusion requirements, haemoglobin and length of stay were assessed using Chi-square and Fisher's exact test as appropriate. Factors associated with ≥2 red cell (RBC) transfusions were explored using bivariate and multivariate logistic regression analysis and expressed as odds ratio (OR) with 95% confidence intervals (CI). **Results**: The mean (SD) age of the cohort was 61 (8) years; 79% were males. Baseline heart rate, body mass index, blood pressure, co-morbidities and creatinine were similar in the treatment (n=45) and control (n=159) arms. The median (IQR) EuroSCORE-II was 0.94 (0.7-1.2) in cases and 0.93 (0.7-1.3) in controls. The median preoperative hemoglobin was 11.6 (11.1-12.5) g/dl and not different (p=0.63) in cases and controls. RBC transfusion requirement was similar (p=0.69) perioperatively in cases (1.38 (1.11) units) and controls (1.46 (1.17)). Fresh frozen plasma (p=0.98) and platelet (p=0.13) transfusions were similar in both groups; 4 patients needed cryoprecipitate. On multivariable logistic regression analysis, female gender (OR 2.76, 95%CI 2.16-14.7), higher EuroSCORE-II (3.77, 1.53-9.31) and longer cross-clamp time (1.04, 1.01-1.06) were independently associated with the need for ≥2 RBC transfusions perioperatively. **Conclusions**: The acute preoperative administration of ultra-short acting iron and vitamin B_{12} in patients undergoing CABG surgery did not reduce perioperative transfusion requirements. Several factors were associated with the need for ≥2 RBC transfusions.

Keywords: Anaemia, transfusion, iron; vitamin B_{12}, outcome, cardio-pulmonary bypass surgery

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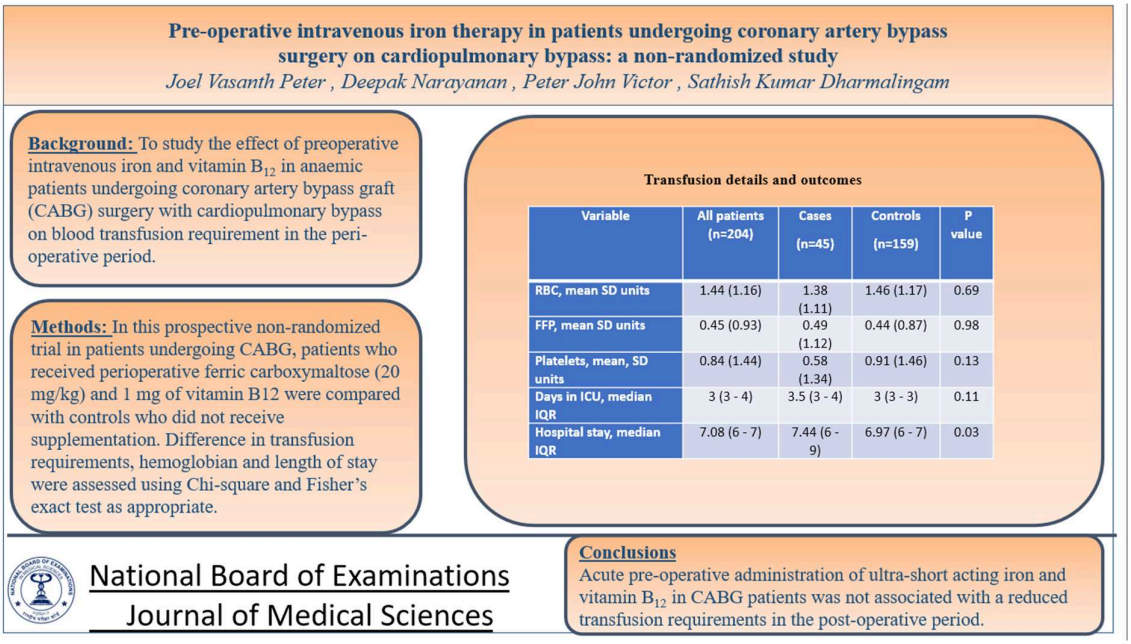
Graphical Abstract



Introduction

Anaemia contributes to perioperative morbidity and mortality in patients undergoing coronary artery bypass graft (CABG) surgery. In a large study from Italy of 4594 patients who underwent CABG, a linear relationship between the severity of anaemia and mortality was demonstrated, with mortality of 3.4% in patients without anaemia and 7.7% and 15.7% in mild and moderate to severe anaemia respectively [1]. In another cohort involving 3500 patients in Canada [2], the prevalence of anaemia, defined as haemoglobin <12.5 g/dl, was 26%. The composite outcome of in-hospital death, stroke, or acute kidney injury (AKI) was significantly higher in patients with anaemia and was independently associated with worse outcomes [2].

Given the association between anaemia and perioperative outcomes in patients undergoing CABG, it appears intuitive to correct anaemia prior to subjecting the patient to surgery. Correction of anaemia would involve assessing the cause and initiating appropriate treatment. Although anaemia due to deficiency (e.g., iron, vitamin B_{12}, folic acid) could be effectively treated with nutritional supplementation, anaemia due to other causes (e.g., chronic kidney disease (CKD), anaemia of chronic disease) may be difficult to correct. Delaying surgery while waiting for the haemoglobin to improve in nutritional deficiencies may pose risk to patients with significant coronary artery disease (CAD).

The gold standard for the treatment of anaemia in the perioperative period is blood transfusions. However, blood transfusions can be associated with early complications such as haemolytic reactions, non-haemolytic febrile reactions, allergies and anaphylaxis, acute lung injury, fluid overload and hyperkalaemia as well as delayed complications such as infections, iron overload and immune sensitisation [3,4]. There is also evidence that the greater

the number of blood transfusions, the higher the mortality and morbidity [3,4].

In this context, there has been interest in the ultra-short-term use of a combination of iron, vitamin B_{12} and erythropoietin prior to surgery. In a single study of 1006 patients with preoperative anaemia or isolated iron deficiency anaemia who were scheduled to undergo cardiac surgery [5], ultra-short-term combination treatment with intravenous iron, subcutaneous erythropoietin alpha, vitamin B_{12} and oral folic acid reduced red blood cell [5] and total allogeneic blood product requirements in the post-operative period, with the effect lasting for 90 days [5].

This non-randomized prospective study was undertaken to evaluate if preoperative administration of intravenous iron carboxymaltose and vitamin B_{12} would reduce perioperative transfusion requirements in patients with anaemia who are undergoing CABG surgery on cardiopulmonary bypass pump when compared with patients who were not treated with supplements.

Patients and Methods

Setting and study design

This prospective non-randomized study was undertaken in a tertiary care teaching hospital in India between September 2021 and November 2022 on patients who were posted for CABG and were found to be anaemic. Anaemia was defined as haemoglobin <12 g/dl in women and <13 g/dl in men. The treatment arm comprised of patients undergoing CABG who consented to participate. They received ferric carboxymaltose intravenously and vitamin B_{12} subcutaneously preoperatively. The control arm did not receive supplements. Although this study was planned as a randomized controlled clinical trial, due to logistic issues, this study was undertaken as a cohort study with two arms.

Inclusion and exclusion criteria

Patients undergoing CABG without any valve replacement with the following characteristics, age 18 – 90 years, ASA 2, 3 and 4 and ejection fraction of >40% were considered for inclusion. Exclusion criteria were those with a known bleeding disorder, revision surgery, ASA 5 and above, age <18 years and >90 years, allergy to intervention drugs, emergency CABG surgery, patients undergoing off-pump CABG, patients with severe anaemia (<8 g/dL), and postoperative revision surgery due to hemopericardium or sternal wound infection.

Patient recruitment

Patient were recruited after they were posted in the elective cardiothoracic surgery list. Patients were approached by the principal investigator (PI) prior to surgery and the study was explained in detail. An information sheet was also provided in the language that they understood. If the patient agreed to participate in the study, signed consent was obtained. Other patients with anaemia, who underwent CABG and who were either unwilling to receive the study drugs or were not recruited due to logistic issues were enrolled to the control arm. The treatment protocol was similar for all patients.

Data collection

Data collected included demographics, treatment details and outcomes. Demographic data included age, gender, height, weight, body mass index (BMI), co-morbidities and habits (smoking, alcohol). Baseline heart rate (HR) and

blood pressure (BP) were recorded. Complete blood examination, renal and liver function tests and coagulation parameters were done preoperatively. EuroSCORE II was calculated for all patients [1].

Intraoperative and postoperative data on the use of inotropes, time of extubation, and length of stay (LOS) in ICU and hospital were recorded. The vasoactive-inotropic score (VIS), a composite index of quantum of vasoactive agents used [6], was calculated for all patients.

The number of units of red blood cells (RBC), platelets, FFP, and cryoprecipitate that were transfused during surgery and postoperative period were recorded. Data sheets were kept in the patient's hospital folder, so that intraoperative details could be filled by the attending anaesthesiologist. It was collected after the patient reached the intensive care unit (ICU) and was followed up by the PI till discharge.

Outcome parameters

The primary outcome was the need for RBC transfusions in the perioperative period. Secondary outcomes included postoperative haemoglobin, duration of mechanical ventilation and ICU and hospital LOS. The need for other blood products (platelets, fresh frozen plasma, cryoprecipitate) was recorded.

Administration of study drugs

The study drugs were administered at least 48-h prior to the surgery. The intravenous iron was given at 20 mg/kg (up to a maximum of 1 g) in 100 ml of normal saline over 2-h under monitoring. Patients also received 1-mg of subcutaneous vitamin B_{12} prior to the iron.

Anaesthesia and surgery protocols

During surgery, intravenous access was established and standard monitoring devices (electrocardiography, pulse oximetry, end-tidal CO_2 monitoring, invasive arterial BP monitor) were placed prior to induction of anaesthesia. The standard protocol involved the intravenous administration of injection fentanyl 2-3 mcg/kg and propofol 1-2 mg/kg, and, vecuronium 0.1 mg/kg or rocuronium 1.5 mg/kg for induction. After intubation, central venous access was obtained through the internal jugular vein using an 8.5 Fr quad lumen. Anaesthesia was maintained with balanced air, oxygen, and isoflurane (0.8 to 1 MAC). Intra-operatively, boluses of fentanyl or morphine were given to decrease the pain response. Paracetamol was also administered intra-operatively.

The BP was titrated intraoperatively with noradrenaline, adrenaline, and glyceryl trinitrate. Hypotension was treated with phenylephrine or ephedrine boluses. The cross-clamp time and the cardio-pulmonary bypass (CPB) time was noted by the perfusionists who were managing the patient during the CPB period intraoperatively. Heparin was given prior to going on CPB based on the body weight and titrated to >3 times the baseline or at least 450 sec.

Blood was transfused based on the haemoglobin on the arterial blood gas (ABG) that was taken at while on bypass and after coming off bypass. The cut-off for transfusion was <7.0 g/dL during CPB and <8g/dL after CPB. After coming off bypass, protamine was administered in the ratio of 1:1.2 to 1:1.4 to bring ACT to baseline. FFP and platelet transfusions intraoperatively were based on clinical parameters such as a wet field with no active bleeder, adhesion of mediastinal structures, preoperative low

platelets, and recent intake of clopidogrel or preoperative liver derangements (rare) and laboratory coagulation parameters done intraoperatively. Once haemostasis was achieved, the patient was transferred to the ICU with the endotracheal tube in situ.

Once extubation criteria were fulfilled, the patient was extubated. The supports were gradually weaned off and, if necessary, blood and blood products were administered according to the laboratory and clinical parameters. Once the patient was stable, he/she was discharged to the ward. When fit for discharge, the patient was asked to review after 3-4 weeks with a repeat haemoglobin.

Statistical methods

Sample size calculations were done as for a randomised trial assuming that 70-80% of anaemic patients would require perioperative RBC transfusion. To detect a 15% difference in the transfusion requirement with supplements, 100 patients needed to be recruited in each arm, assuming 80% power. Summary data was presented as mean (standard deviation, SD) for continuous variables with normal distribution and as median with interquartile range (IQR) if data was skewed. Categorical variables were presented as numbers and percentages The difference in transfusion requirements, haemoglobin and length of stay were assessed using Chi-square and Fisher's exact test as appropriate. Factors associated with need for ≥2 RBC transfusions were explored using bivariate logistic regression analysis and reported as unadjusted analysis. Clinically and statistically significant factors were incorporated in a multivariable logistic regression analysis. Statistical significance was defined as $p<0.05$. All analyses were performed using Statistical Package for Social Sciences for Windows (SPSS) v25 and STATA™ v16.

IRB and ethics committee approval details

The study was approved by the Institutional Review Board (IRB No. 13821, 24.02.2021). The interventional medications were provided from the approved funds.

Results

Baseline characteristics

During the study period, 723 patients were screened. Of these, 519 patients were excluded (Figure 1). Of the 204 patients who were considered suitable for inclusion, 159 did not receive the intervention and were taken as controls (control arm). Of the 65 patients who consented to participate in the trial, 45 received the intervention (treatment arm); 18 patients were excluded due to cancellation of surgery, re-exploration and surgeon unwilling for patient to receive the intervention. Another 2 patients were lost to follow up.

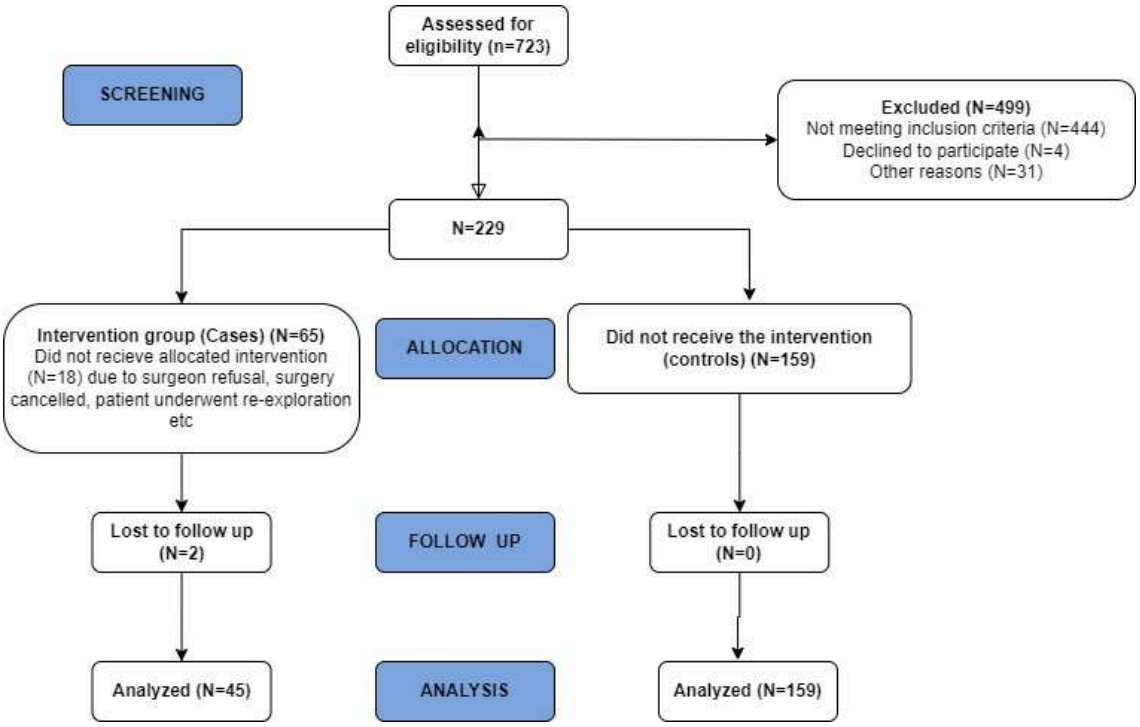


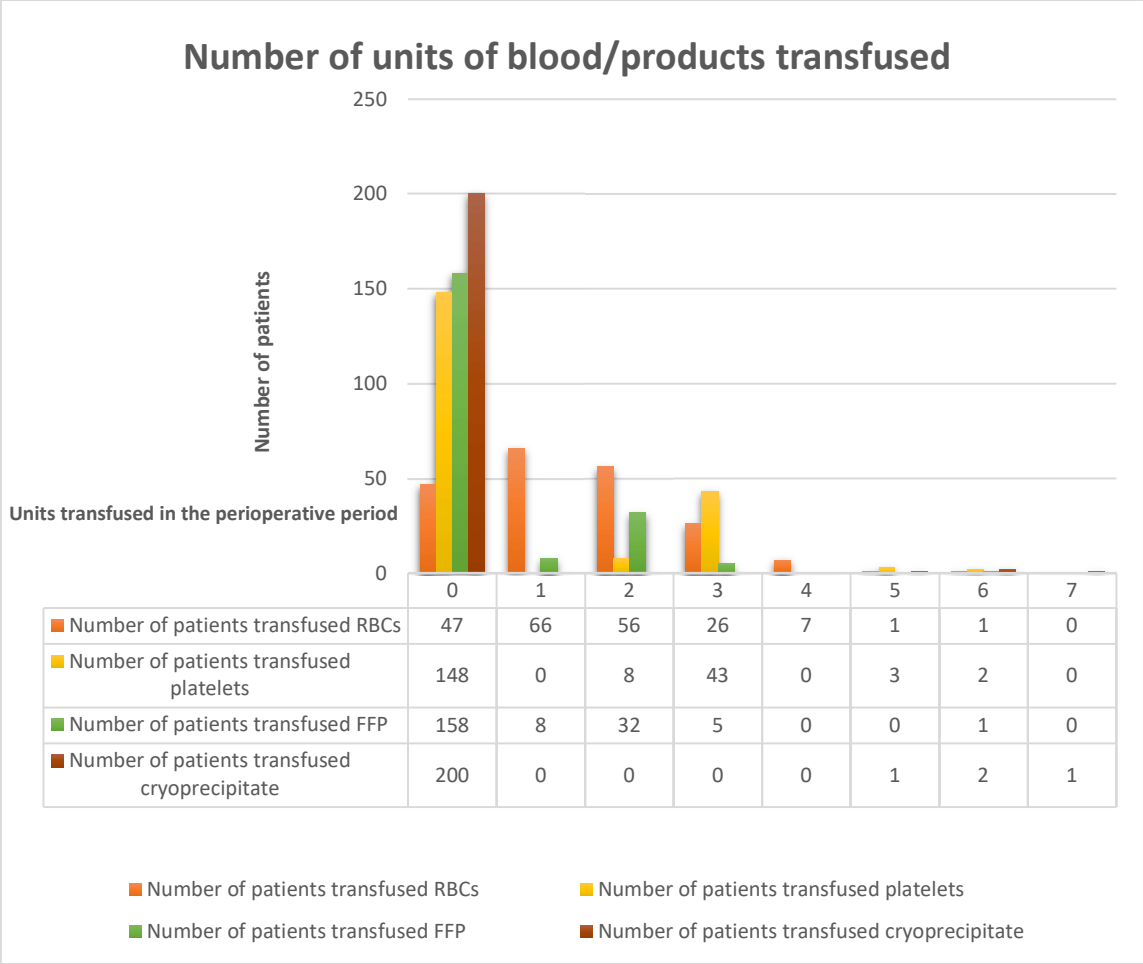
Figure 1. Strobe diagram of patients screened and included.
Strobe diagram shows the number of patients who were screened and the number who were finally analysed. Of the 723 patients who were assessed for eligibility, 499 patients were excluded for not meeting inclusion criteria (n=444), declining to participate (n=4) and other reasons (n=31). Of the remaining 224 patients, 65 were included in the treatment group. Of these, 18 did not receive the treatment and 2 patients were lost to follow-up. The treatment arm hence had 45 patients. The remaining 159 patients were controls

(SD) serum creatinine was 1.1 mg/dL (0.86). When patients were categorized according to the ASA grade, a majority (81.4%) were Grade 3. A majority (73%) had normal left ventricular ejection fraction (EF) and 27% had mild left ventricular systolic dysfunction (EF 40-49%).

Treatment details

All patients had significant obstruction of the left anterior descending artery that required grafting. The other vessels that were grafted were obtuse marginal artery (n=167), posterior descending artery (n=87), right coronary artery (n=33), diagonal branches (n=29), ramus intermedius (n=27) and the postero-lateral artery (n=9).

Transfusion details are summarized in Figure 2. Overall, 47 patients did not require RBC transfusion; the rest required between one and six units of transfusion, with a majority (n=66) requiring one unit during surgery (Figure 2). Platelet transfusion was required in 56 patients (2 units 8 patients, 3 units 43 patients). FFP was transfused in 46 patients; a majority required two units of FFP while 13 patients required either 1 or 3 units. Cryoprecipitate was required in 4 patients (2 %).



	0	1	2	3	4	5	6	7
Number of patients transfused RBCs	47	66	56	26	7	1	1	0
Number of patients transfused platelets	148	0	8	43	0	3	2	0
Number of patients transfused FFP	158	8	32	5	0	0	1	0
Number of patients transfused cryoprecipitate	200	0	0	0	0	1	2	1

Figure 2. Blood product transfusions

Figure shows the number of patients who received the specific units of transfusion in the y axis. The x axis denotes the number of units transfused (ranging from 0 to 7) of a product (red blood cell (RBC), fresh frozen plasma (FFP), platelets and cryoprecipitate), each of which is colour coded. Of the 204 patients in the study, no RBC transfusion was required in 47 patients, while no platelets, FFP and cryoprecipitate transfusions were required in 148, 158 and 200 patients respectively. One unit of RBC transfusion was required in 66 patients while 56 patients required 2 units; 35 patients needed 3 or more RBC transfusions.

Comparison of cases and controls

Exploratory analysis was undertaken to compare several variables between cases and controls. Baseline characteristics and comorbidities were similar in the treatment and control arms (Table 1). Clinical variables, baseline investigations and EUROSCORE-II were also not different between cases and controls (Table 2). The low EUROSCORE-II suggests that patients were low risk for surgery.

The mean (SD) number of RBCs that was transfused was 1.4 (1.16) units (Table 3). There was no significant difference in the number transfused between cases and controls (p=0.69). Since the primary outcome was not different between cases and controls, no further exploratory analysis was performed. The

requirement of FFP was only 0.45 (0.93) units and similar between the two groups (p=0.98). Similarly, the requirement of platelets was 0.84 units (1.44) and not different between cases and controls (p=0.13).

Table 1. Summary of baseline characteristics between cases and controls

Variable	All patients (n=204)	Cases (n=45)	Controls (n=159)	P value
Age, mean (SD) years	61.0 (8)	60.5 (8.4)	61.0 (7.9)	0.67
Gender, M: F (% M)	162:44 (79.0)	33:12 (73.3)	129:31(80.6)	0.29
Height, mean (SD) cm	161.6 (8.7)	161.2 (8.7)	161.7 (8.8)	0.73
Weight, mean (SD) kg	63.3 (10.6)	63.2 (10.6)	63.3 (10.6)	0.95
BMI, mean (SD) kg/m2	24.3 (3.29)	24.5 (3.35)	24.2 (3.28)	0.67
Diabetes mellitus	144 (70.6)	33 (73.3)	111 (69.8)	0.71
Hypertension	143 (70.1)	27 (60.0)	116 (74.9)	0.10
Bronchial asthma	5 (2.5)	1 (2.2)	4 (2.5)	1.0
Chronic kidney disease	8 (3.9)	3 (6.7)	5 (3.9)	0.38
Dyslipidaemia	26 (12.8)	7 (15.6)	19 (12.0)	0.61

SD – Standard deviation

Table 2. Clinical and laboratory variables at recruitment

Clinical variables	All patients (n=204)	Cases (n=45)	Controls (n=159)	P value
Heart rate, beats/min	74.6 (65 - 85)	75.3 (65 - 85)	74.4 (65 - 85)	0.71
Systolic BP (mm Hg)	135 (120 - 150)	134 (120 - 140)	135 (120 - 150)	0.61
Diastolic BP (mm Hg)	80.0 (70 - 85)	79.4 (70 - 85)	80.1 (70 - 85)	0.67
MAP, mean, SD	98.3 (9.5)	97.7 (8.5)	98.5 (9.8)	0.63
EUROSCORE-II	0.93 (0.7 - 1.3)	0.94 (0.7 - 1.2)	0.93 (0.7 - 1.3)	0.40
Haemoglobin, g/dl	11.6 (11.1 - 12.5)	11.5 (11.1 - 12.3)	11.7 (11.2 - 12.6)	0.63
MCV, mean, SD	86.0 (81.6 – 91.0)	85.6 (81.1 - 90.5)	86.1 (82.7 - 91.4)	0.70
Platelets (x 10^5)	2.21 (1.54 – 2.67)	2.32 (1.81 – 2.73)	2.81 (1.51- 2.66)	0.23
PT	14.4 (13.5 - 15.2)	14.6 (13.4 - 15.4)	14.4 (13.6 - 15.1)	0.51
PT (INR)	1.07 (0.99 - 1.12)	1.07 (0.97 - 1.15)	1.06 (0.99 - 1.11)	0.55
APTT	34.1 (30.9 - 36.1)	33.2 (30 - 36.1)	34.4 (31.1 - 36.1)	0.19
Creatinine	1.11 (0.82 - 1.16)	1.04 (0.78 - 1.09)	1.13 (0.83 - 1.17)	0.53
Creat. clearance	71.7 (54.1 - 86.9)	72.7 (53.8 - 91.8)	71.5 (54.1 - 86.1)	0.78

All values are median interquartile range unless specified, MAP mean arterial pressure, MCV mean corpuscular volume, PT prothrombin time, INR international normalized value, APTT activated partial thromboplastin time, SD standard deviation.

Table 3. Transfusion details and outcomes

Variable	All patients (n=204)	Cases (n=45)	Controls (n=159)	P value
RBC, mean SD units	1.44 (1.16)	1.38 (1.11)	1.46 (1.17)	0.69
FFP, mean SD units	0.45 (0.93)	0.49 (1.12)	0.44 (0.87)	0.98
Platelets, mean, SD units	0.84 (1.44)	0.58 (1.34)	0.91 (1.46)	0.13
Days in ICU, median IQR	3 (3 - 4)	3.5 (3 - 4)	3 (3 - 3)	0.11
Hospital stay, median IQR	7.08 (6 - 7)	7.44 (6 - 9)	6.97 (6 - 7)	0.03

SD standard deviation; IQR interquartile range, RBC red blood cell transfusion, FFP fresh frozen plasma, ICU intensive care unit.

The duration of ICU stay was similar between cases and controls (p=0.11). However, the duration of hospital stay post-surgery was marginally but significantly higher in controls (P=0.03) when compared with cases.

Factors associated with more than one unit of RBC transfusion

Exploratory analysis was undertaken to evaluate for factors associated with the need for >2 units of RBC transfusion. On bivariate logistic regression analysis (Table 4a), factors associated were increasing age (OR 1.05, 95%CI 1.02 to 1.10), female gender (OR 3.95, 95%CI 1.92 to 8.12), higher EuroSCORE-II (OR 3.50, 95%CI 1.84 to 6.67), pre-operative haemoglobin (OR 5.64, 95%CI 2.72 to 11.72), cross-clamp time (OR 1.02, 95%CI 1.0 to 1.04), number of platelets transfused (OR 1.35, 95%CI 1.11 to 1.65) and number of FFP transfused (OR 1.73, 95%CI 1.23 to 2.43). The need for ≥2 RBC transfusion was associated with longer duration of hospital stay following surgery (OR 1.19, 95%CI 1.04 to 1.36) but not with increased ICU LOS (OR 1.14, 95%CI 0.69 to 1.91).

On multivariable logistic regression analysis (Table 4b), female gender (OR 2.76, 95%CI 2.16 to 14.7), higher EuroSCORE II (OR 3.77, 95%CI 1.53 to 9.31) and longer cross-clamp time (OR 1.04, 95%CI 1.01 to 1.06) were independently associated with need for 2 or more units of RBC transfusion during the perioperative period. Platelet and FFP transfusions were not incorporated in the model due to co-linearity in the relationship between the need for red cells and platelet and FFP transfusions.

Table 4 a. Bivariate analysis of factors associated with ≥2 RBC transfusion.

Variable	Odds ratio	95% confidence interval	P value
Age	1.05	1.02 to 1.10	0.006
Female gender	3.95	1.92 to 8.12	<0.001
EuroSCORE II	3.50	1.84 to 6.67	<0.001
NYHA class of symptoms	1.28	0.52 to 3.14	0.59
Number of vessels diseased	1.61	0.83 to 3.15	0.16
Ejection fraction on ECHO	1.00	0.96 to 1.04	0.97
Pre-operative haemoglobin~	5.64	2.72 to 11.72	<0.001

Pre-operative iron/vitamin B12^	1.00	0.52 to 1.95	0.99
Baseline MAP	0.97	0.95 to 1.00	0.09
Baseline heart rate	1.02	1.00 to 1.05	0.11
Time on CPB	1.01	1.00 to 1.02	0.11
Cross clamp time	1.02	1.00 to 1.04	0.054
Vasoactive inotrope score	1.04	0.93 to 1.16	0.51
Number of platelets transfused	1.35	1.11 to 1.65	0.003
Number of FFP transfused	1.73	1.23 to 2.43	0.002
Duration of ICU stay	1.14	0.69 to 1.91	0.59
Duration of hospital stay*	1.19	1.04 to 1.36	0.012

Table 4b. Multivariate analysis of factors associated with ≥2 RBC transfusion.

Variable	Odds ratio	95% confidence interval	P value
Age	1.03	0.98 to 1.08	0.31
Female gender	2.76	2.16 to 14.7	<0.001
EuroSCORE II	3.77	1.53 to 9.31	0.004
Cross clamp time	1.04	1.01 to 1.06	0.006
Duration of hospital stay	1.02	0.87 to 1.23	0.71

*Hospital stay is post-surgery; MAP mean arterial pressure, CPB cardiopulmonary bypass; ICU intensive care unit; FFP fresh frozen plasma; NYHA New York Heart Association; ^peri-operative administration of iron/vitamin B_{12}

Discussion

In this non-randomized study of patients with anaemia and undergoing CABG using CPB, acute preoperative administration of iron and vitamin B_{12} did not reduce transfusion requirements in the perioperative period. The mean number of RBC transfusion was similar in the treatment (1.38, SD 1.11) and control (1.46, 1.17) arms as was the requirement for FFP (p=0.98) and platelets (p=0.13). On multivariable logistic regression analysis, female gender (OR 2.76, 95%CI 2.16 to 14.7), higher EuroSCORE-II (OR 3.77, 95%; CI 1.53 to 9.31) and longer cross-clamp time (OR 1.04, 95%CI 1.01 to 1.06) were independently associated with the need for ≥2 RBC transfusions perioperatively.

It is recognized that anaemia is not infrequent in patients with CAD and that it can contribute to perioperative morbidity and mortality in those undergoing CABG surgery. In the cohort study from Canada enrolling 3500 patients undergoing CABG, the prevalence of preoperative anaemia was 26% [2]. Anaemia was significantly associated with in-hospital death, stroke, and AKI [2]. In the study from Italy that included 4594 patients, the mortality was 3.4% in patients without anaemia while it ranged from 7.7 to 15.7% in those with mild and moderate to severe anaemia [1]. Thus, there appears to be merit in correcting anaemia in the preoperative period.

Over the last decade, several observational, retrospective, and prospective studies have evaluated the role

of pre-operative therapy with iron, vitamin B_{12}, folate and erythropoietin [6-10] (Table 5). The timing of administration ranged from 1 day to 4-6 weeks pre-operatively. In our cohort, iron, and vitamin B12 were administered within 48-h of surgery. Although it is likely that a long lag time from supplemental therapy to surgery would reduce need for transfusion in the peri-operative period, two studies, did not demonstrated a reduction in transfusion requirements. In an observation study by Klein et al. [7], treatment with iron at a median (IQR) of 33 (15-53) days prior to surgery was not associated with a reduction in the proportion of patients needing transfusion ($p=0.127$). In another retrospective study by Quarterman et al (8), administration of iron 4-6 weeks prior surgery was not associated with a reduction in the median units of transfusion required in the peri-operative period ($p=0.24$). On the other hand, 3 studies [5,9,10] showed a beneficial effect on transfusion despite iron and/or erythropoietin and vitamin B_{12} and folate being given within 7 days of surgery. The study by Jafari et al. [8] showed a significant reduction ($p<0.001$) in the requirement for transfusion (Table 5). Shokri et al. [9] showed a significant ($p<0.001$) reduction in the proportion of patients requiring transfusion. In the largest randomized controlled trial done on this subject [5], a significant reduction in need for transfusion was demonstrated.

Table 6 summarizes the key differences between the largest randomized trial on supplemental iron with the current study. Patients in our study were slightly younger, had a lower BMI and lower proportion of females and less smoking and alcohol use when compared to the Lancet study [5]. A larger proportion of patients in the current study had prior myocardial infarction. The EuroSCORE II was much lower in our cohort suggesting that our patients had low risk. The pre-operative haemoglobin was lower in the current study when compared to the Lancet study [5], while pre-operative platelet count and creatinine were similar.

The number of RBCs that were required was slightly higher in the Lancet study. In the Lancet study (5), in the treatment group, the mean (SD) units transfused in the first 90 days was significantly lower ($p=0.018$) at 1.7 (3.2) units, while in the control group it was 2.3 (3.3). In our study, 1.38 (1.11) units were transfused in the treatment group and 1.46 (1.17) in the control group ($p=0.69$). The difference between the two studies is likely to be the power of study, with the current study probably underpowered to detect a significant difference.

The lower transfusion requirement in our cohort when compared with the Lancet cohort could be attributed to younger population, lower EuroSCORE-II, less co-morbidities, and a lower proportion of females. The two studies also differ from the fact that patients in the Lancet study additionally received erythropoietin. The timing of administration of these agents were within 7 days in both groups however in our study it was within 48 hours. Our cohort was less heterogeneous with the inclusion of only patients who underwent CABG graft surgery on bypass while the Lancet study had a more heterogeneous group of patients who underwent CABG bypass graft surgery and valvular surgeries on bypass as well as off bypass.

Table 5. Summary of studies on pre-operative iron

Study	Type	Intervention, timing	Outcome	Rx (n)	Control (n)	Outcome		P value
						Rx	Control	
Current study, India 2022	Non-randomized prospective study	20 mg/kg of ferric carboxymaltose and 1 mg of subcutaneous vitamin B12 within 48 h of surgery	Mean (SD) units transfused	45	159	1.38 (1.11)	1.46 (1.17)	0.69
Jafari S et al, Tehran 2022 (9)	RCT	Iron sucrose 200 mg Erythropoietin 100 IU/Kg, 1-2 days prior to surgery	Mean (SD) units transfused	57	57	1.53 (1.04)	2.56 (1.35)	<0.001
Klein AA et al, UK 2020 (7)	Observational	Iron isomaltoside or ferric carboxymaltose 20 mg/kg at median (IQR) of 33 days (15-53)	Proportion needing transfusion	64	72	31 (56%)	28 (42%)	0.127
Shokri H et al, Egypt 2022 (10)	Randomized trial	Ferric carboxymaltose 1000 mg single dose, 7 days prior to surgery	Proportion needing transfusion post-op	40	40	5 (12.5%)	22 (55%)	<0.001
Quarterman C et al, UK 2021 (8)	Retrospective review	Iron isomaltoside 1000 mg, 4 to 6 weeks prior to surgery	Median (IQR) units transfused	190	581	2 (1-3)	2 (1-4)	0.24
Spahn DR et al, Switzerland 2019 (5)	RCT	20 mg/kg ferric carboxymaltose, 40 000 U erythropoietin alpha s/c, 1 mg s/c vitamin B12, 5 mg oral folic acid on the day before surgery	Mean (SD) units transfused in the first 90 days	243	241	1.7 (3.2)	2.3 (3.3)	0.018

RCT randomized controlled trial; SD standard deviation; IQR interquartile range; Rx treatment group; s/c subcutaneously

Table 6. Comparison of the current study with the Lancet study [5]

Variable	Lancet study		Current study	
	Cases n=243	Controls n=241	Cases n=45	Controls n=159
Demographic data				
Age	69 (11)	67 (12)	60.5 (8.4)	61.0 (7.9)
Females, (%)	85 (35%)	82 (34%)	12 (27%)	31 (19%)
Height, (cm)	168 (9)	169 (10)	162.7 (8.7)	161.7 (8.8)
Weight, (kg)	76 (15)	77 (16)	63.2 (10.6)	63.3 (10.6)
BMI	27.1 (4.8)	26.9 (5.0)	24.5 (3.4)	24.2 (3.3)
History of MI, (%)	66 (28%)	63 (26%)	16 (36%)	51 (32%)
Habits				
Alcohol use, (%)	53 (22%)	49 (20%)	6 (13%)	23 (11%)
Smoker, (%)	126 (52%)	131 (54%)	11 (25%)	49 (31%)
Tobacco chewer, (%)	NA	NA	7 (16%)	14 (9%)
Scoring				
EUROSCORE II	4.5 (5.3)	4.2 (4.8)	0.94 (0.43)	0.93 (0.76)
Hemodynamic variables				
Heart rate, per min	NA	NA	75.3 (11.5)	74.4 (11.3)
SBP, mmHg	131 (22)	130 (20)	134 (15)	135 (16)
DBP, mm Hg	72 (12)	70 (12)	79.4 (8.5)	80.1 (8.8)
Laboratory variables				
Pre-op Hb, (gm/dl)	12.8 (1.5)	12.9 (1.5)	11.8 (1.2)	11.7 (1.2)
Platelet count, x 10^5	2.4 (73000)	2.27 (66000)	2.32 (78073)	2.81 (93474)
Creatinine, (mg/dl)	1.01 (0.28)	1.01 (0.29)	1.04 (0.45)	1.13 (0.94)
Transfusion details				
No. of RBC transfused	1.7 (3.2)	2.3 (3.3)	1.38 (1.11)	1.46 (1.17)
No. of FFP transfused	0.1 (1.1)	0.2 (1.7)	0.49 (1.12)	0.44 (0.87)
No. Platelets transfused	0.3 (1.1)	0.3 (1.2)	0.58 (1.34)	0.91 (1.46)

All values are mean (standard deviation) unless specified; Hb haemoglobin; NA not available; No. number; BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, MI myocardial infarction; RBC red blood cell, FFP fresh frozen plasma.

The study must be interpreted in the light of the following limitations. First and foremost, the COVID-19 pandemic resulted in lockdown and severe economic consequences because of which patient load decreased significantly. This resulted in the inability to recruit more patients. There was a delay in procurement of the study drug which also restricted the number of patients who could be recruited during the period of the study. This study was initially planned as a randomized trial. However, there was much reluctance among surgeons on the probable adverse effects of the intravenous administration of iron pre-operatively, particularly in patients with triple vessel disease and those with a high degree of occlusion. This was probably due to limited prior use of intravenous iron in the pre-operative period in this clinical setting. This resulted in the inability to follow the randomization protocol and allocation concealment due to the uncertainty if permission would be given to administer

iron after recruitment. In view of this, the study design was changed to a cohort, non-randomized study. This limits the ability to ensure that known and unknown factors were balanced in both the treatment and control arms. However, despite this, it was interesting to note that the treatment and control arms had similar baseline characteristics as well as EuroSCORE-II.

CONCLUSIONS

In this non-randomized study of patients with anaemia and undergoing CABG using CPB, preoperative administration of iron and vitamin B_{12} did not reduce transfusion requirements in the perioperative period. Female gender, higher EuroSCORE-II and longer cross-clamp time were independent risk factor for the need for 2 or more RBC transfusions in the perioperative period. Larger studies may provide definitive answers for the role of preoperative supplementation of iron and vitamin B_{12}.

Statements and Declarations

Conflict of interest statement

There was no conflict of interest for all the authors listed in this submission.

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ORIGINAL ARTICLE

Correlation Between Serum Uric Acid Levels and Metabolic Syndrome in Adults

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Abstract

Background: Metabolic syndrome is a group of metabolic abnormalities, and these abnormalities are associated with an increased risk of cardiovascular disease and DM. Due to surge in prevalence of obesity in young adults, the prevalence of metabolic syndrome will likely rise significantly in near future. The serum uric acid levels are significantly raised in metabolic syndrome and are associated with adverse cardiovascular mortality. **Aim:** This study aims to investigate correlation between serum uric acid levels and metabolic syndrome. **Discussion:** Existing studies showed positive correlation of hyperuricemia with metabolic syndrome in elderly patients. But there is limited research on uric acid levels in young population with obesity, hypertension and metabolic syndrome. Consequently, a cross-sectional observational study was conducted on metabolic syndrome patients and their correlation with serum uric acid levels. **Conclusion:** This study showed significant correlation with metabolic syndrome and serum uric acid levels in young adult patients. This higher serum uric acid levels in young adults of metabolic syndrome are rising a concern for cardiovascular adverse outcomes in these young population.

Keywords: Metabolic syndrome, Serum uric acid, Dyslipidaemia

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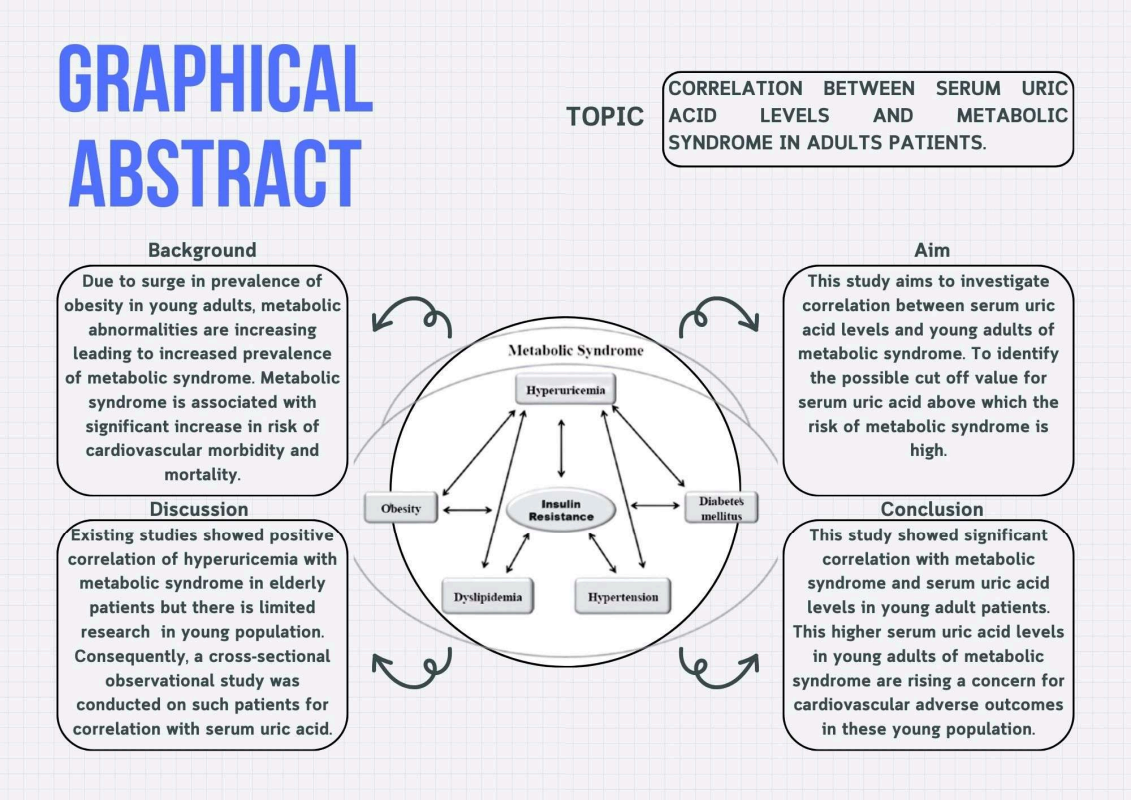
Abbreviations

FBS	:	Fasting Blood Sugar
CVD	:	Cardiovascular Disease
LDL	:	Low Density Lipoprotein
SBP	:	Systolic Blood Pressure
DM	:	Diabetes Mellitus
TGs	:	Triglycerides
BMI	:	Body Mass Index
DBP	:	Diastolic Blood Pressure
HDL	:	High Density Lipoprotein



Introduction

Metabolic syndrome is a group of metabolic abnormalities, and these abnormalities are central obesity, raised blood pressure, insulin resistance, dyslipidaemia, proinflammatory and prothrombotic states [1].

Worldwide, the prevalence of metabolic syndrome (Metabolic syndrome) ranges from 10% to 84%. In India, adult population overall had a 30% prevalence rate of metabolic syndrome [2].

Uric acid, a compound formed due to purine metabolism has been found to be associated and significantly correlated to CVDs. Additionally, impaired glucose tolerance further increases the risk of mortality and morbidity with adverse CVD outcomes [3]. Since the uric acid range is lower in the females it tends to get more positively correlated but at the same time

males has been found to have higher association with risk factors like alcoholism. Also, hormonal factors like oestrogen have been found to be protective in females against metabolic syndrome but after menopause risk remains equal [4].

Pathophysiology

The unhealthy food habits and sedentary lifestyle along with genetic and epigenetic causes play a significant role in pathogenesis of metabolic syndrome. Since most of the metabolic syndrome pathways has been found to be triggered by central adiposity, high caloric intake can be attributed a causal role [5]. The chronic inflammatory state, neurohormonal activation and insulin resistance are crucial elements in the development of metabolic syndrome and its eventual transformation into Type 2 DM and CVDs. Initially normoglycaemia is maintained by compensatory hyperplasia of beta cell mass and increased insulin secretory capacity. Eventually, beta cell dysfunction after a few years led to development of type 2 DM [6].

Obesity can lead to development of hyperuricemia by increasing synthesis of uric acid and decreasing its excretion through kidneys. On the other hand, hyperuricemia can cause obesity by increasing peripheral and hepatic lipogenesis. This obesity and hyperuricemia are substantial risk factors for development of DM [7].

It has been established that hyperuricemia results in loss of endothelial cell function. The lack of endothelial formed nitric oxide lowers blood flow to cells, which inhibits the action of insulin leading to hyperinsulinemia. This insulin resistance plays a vital role in Metabolic syndrome. Serum uric acid and triglycerides have a positive correlation with risk factors related to complications of DM [8].

Hyperuricemia and adverse CVD

Hyperuricemia is significantly associated with hypertension, dyslipidaemia, CVD and heart failure. In congestive heart failure, uric acid serves as an independent predictor of adverse outcomes in elderly hospitalized patients [9]. Epidemiological studies have showed significant increased cardiovascular risks among patients of gout, but there is still controversy that uric acid lowering therapy may benefit from adverse cardiovascular outcomes. Additional research is needed for uric acid lowering therapy in metabolic syndrome and whether to consider uric acid levels as a predictor or marker of metabolic syndrome [10].

Methodology

Study population: Patients older than 18 years of age coming to a tertiary hospital.

Sample size: 181 patients were recruited out of which 91 were males and 90 were females.

Inclusion criteria

- Age > 18 years
- Age < 60 years
- Informed consent
- Metabolic syndrome criteria fulfilled

Exclusion criteria

- Chronic renal failure
- Undergoing renal replacement therapy
- Acute or chronic gout
- Recent history of diuretics intake
- Malignancy

- Stroke
- History of CVD
- Drug history like antiepileptics steroid or recreational drugs
- Pregnancy
- Lactation
- Consent not given

Material and methods

3 ml of blood sample was taken for fasting blood sugar, lipid profile and uric acid. It was processed in fully automated biochemistry analyser XL 1000.

Metabolic syndrome was defined on basis of National cholesterol education programme guidelines as shown in Figure 1 [11].

Glucose Oxidase-Peroxidase method was used to measure fasting blood sugar. In this method, Glucose oxidase breaks down glucose and in turn forms hydrogen peroxide which reacts with peroxidase causing the colour dye to change its colour [12].

For triglycerides, colorimetric enzymatic method with glycerophosphate oxidase was used. This technique follows enzymatic hydrolysis of TGs, and the byproduct gets oxidised by glycerol phosphate leading to generation of a colorimetric reaction. Since it's a quantitative method, colour intensity is directly proportional to the concentration of triglycerides and spectrophotometer is used to measure it [13].

HDL was measured by direct modified polyvinyl sulfonic acid and polyethylene glycol methyl ether method. It is also an enzymatic method which specifically quantifies HDL and is hence an effective method to measure it without having a hindrance from other lipoproteins [14].

Uric acid is quantified with the help of uricase method in which the uricase enzyme forms allantoin by oxidation of uric acid and a colorimetric reaction is generated which can be measured with a spectrophotometer [15].

Results

This study was conducted among 181 patients who presented to GMSH, sector 16, Chandigarh. Among 181 patients 91 were males and 90 were females. Gender wise distribution of uric acid levels is shown in Table 1 and graphically represented in Figures 2 to 4. The normal uric acid is taken as ≤6.5 mg/dL for females and ≤7.5 mg/dL for males.

Among the 181 total participants, 76.8% (n=139) had uric acid levels within the normal range, while 23.2% (n=42) had elevated levels. A higher proportion of males (86.8%) had uric acid within the normal range compared to females (66.7%). Conversely, elevated uric acid levels were more common in females (33.3%) than in males (13.2%). The Chi-Square value of 10.306 and a p-value of 0.001 indicate a statistically significant difference between males and females in terms of uric acid levels, suggesting a potential gender-based variation in hyperuricemia prevalence.

Risk factors	Defining levels
Abdominal obesity	Waist circumference
Men	>102 CM (40 in)
Women	>88 CM (35 in)
Triglycerides	≥ 150 mg/dl
HDL cholesterol	
Men	< 40 mg/dl
Women	<50 mg/dl
Blood pressure	≥ 130/≥ 85 mmHg
Fasting glucose	≥ 110 mg/dL

Figure 1. Metabolic syndrome criteria

Table 1. Uric acid levels gender wise distribution

Uric Acid	Gender						Chi Square	p-value
	Male		Female		Total			
≤6.5 F or ≤7.5 M	79	86.8%	60	66.7%	139	76.8%	10.306	.001
>6.5 F or >7.5 M	12	13.2%	30	33.3%	42	23.2%		
Total	**91**	**100.0%**	**90**	**100.0%**	**181**	**100.0%**		

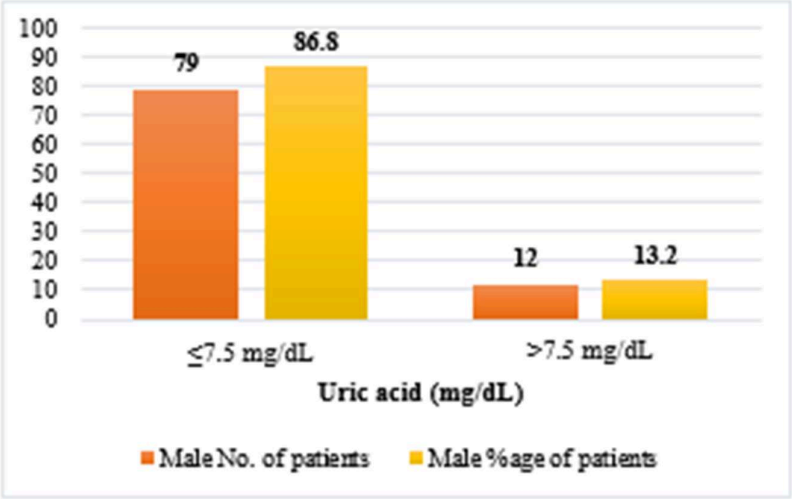


Figure 2. Distribution of uric acid in males

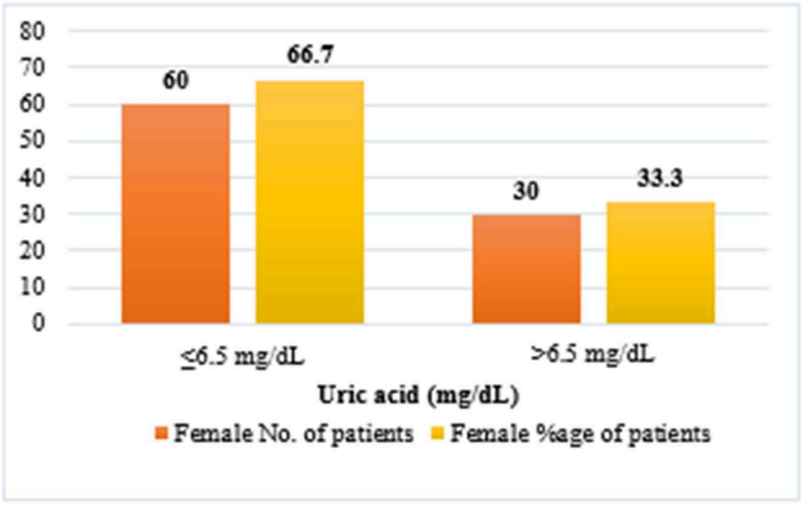


Figure 3. Distribution of uric acid in females

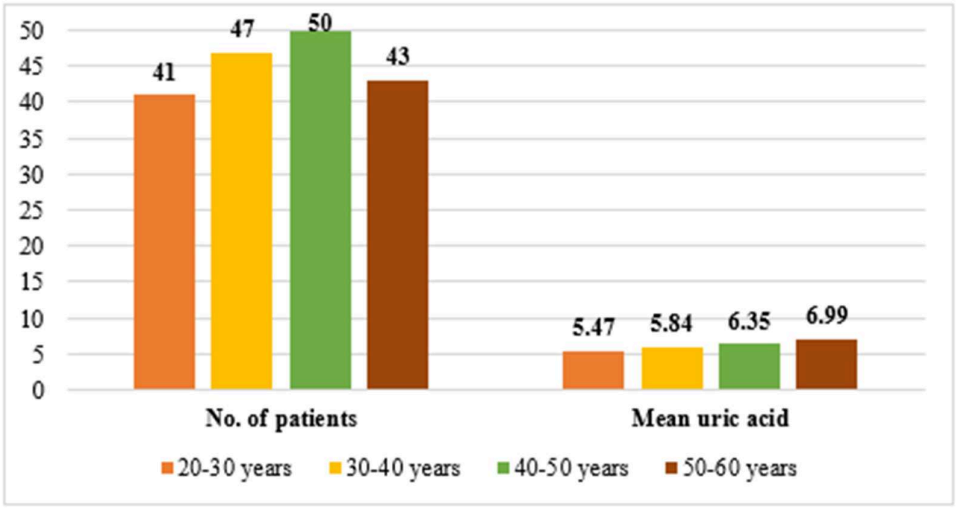


Figure 4. Age wise distribution of patients with their uric acid levels

Table 2. Components of metabolic syndrome correlation with uric acid

Parameters	Uric Acid		
	Pearson coefficient	p-value	No. of patients
Waist circumference	.301	<0.001	181
SBP	.274	<0.001	181
DBP	.391	<0.001	181
FBS	.256	<0.001	181
Total Cholesterol	.405	<0.001	181
TGs	.273	<0.001	181
HDL	-.048	<0.518	181

Correlation of metabolic syndrome and its components with uric acid levels in 181 patients is shown in Table 2 and graphically represented in Figures 5 to 10.

Pearson coefficient indicate a positive correlation between uric acid levels and waist circumference [r=0.301, p<0.001], SBP [r=0.274, p<0.001], DBP [r=0.391, p<0.001], FBS [r=0.256, p<0.001], total cholesterol [r=0.405, p<0.001], and TGs [r=0.273, p<0.001] and all were statistically significant. These results suggest that higher uric acid is associated with worsening metabolic parameters. In contrast, HDL showed a negative correlation [r= -0.048, p= 0.518], although it was statistically insignificant.

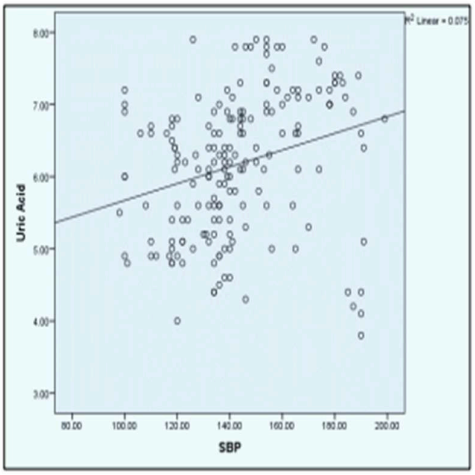


Figure 5. Scatter plot of SBP vs Uric acid

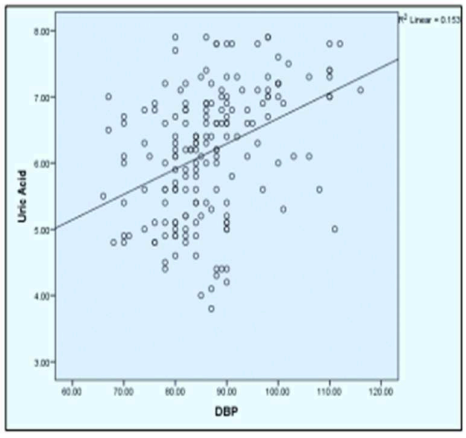


Figure 6. Scatter plot of DBP vs Uric acid

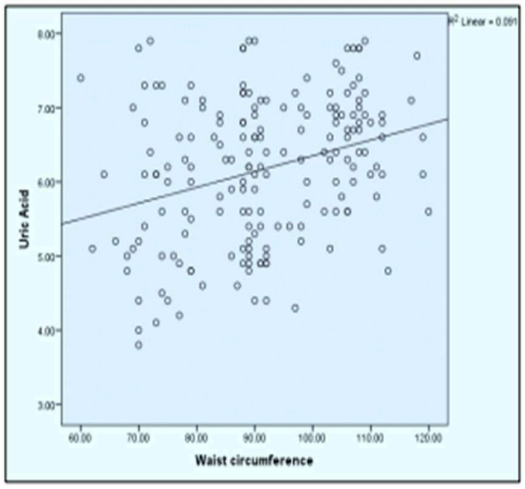


Figure 7. Scatter plot of Waist circumference vs Uric acid

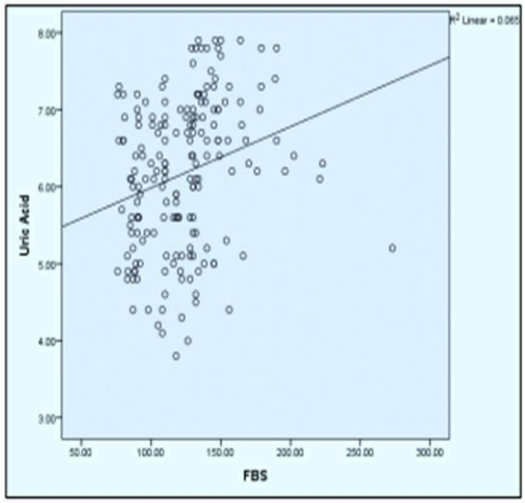


Figure 8. Scatter plot of FBS vs Uric acid

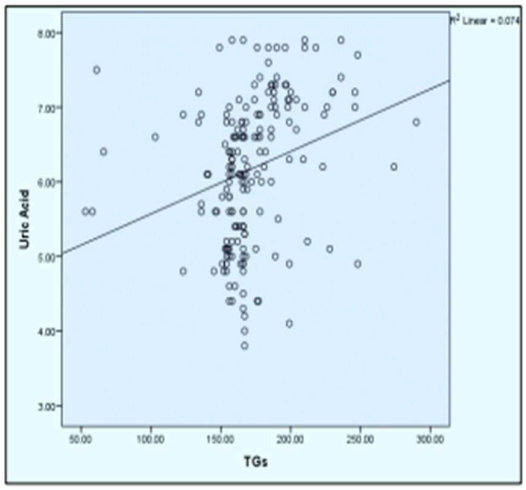


Figure 9. Scatter plot of TGs vs Uric acid

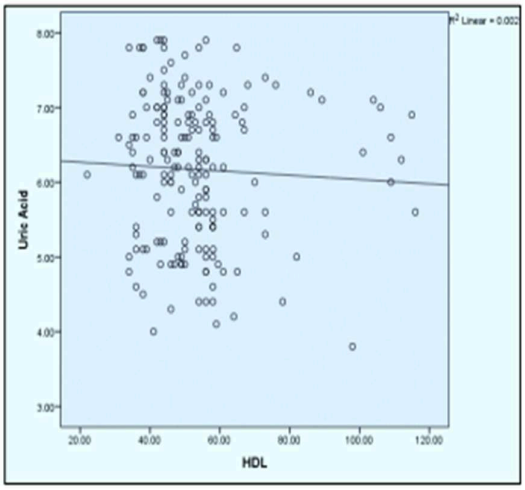


Figure 10. Scatter plot of HDL vs Uric acid

Conclusion

This study shows that elevated uric acid was correlated with metabolic syndrome, linking it to insulin resistance, obesity, hypertension, and dyslipidaemia. Regular monitoring of uric acid may help in early risk assessment, and further research is needed to explore its potential as a therapeutic target.

Future scope

Uric acid can be explored as a predictive biomarker for metabolic syndrome in future. Investigating its role in insulin resistance, hypertension, and dyslipidaemia may lead to targeted therapies. Further studies on genetic factors, lifestyle interventions, and AI-based predictive models could enhance risk assessment and treatment strategies.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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ORIGINAL ARTICLE

Transforming Orthopaedic care with Interprofessional Education: Challenges, Strategies, and Outcomes

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Abstract

Introduction: Interprofessional education (IPE) is critical to improve teamwork and collaboration in orthopaedics, so ultimately improving patient care. This study is about the integration of IPE into orthopaedic practice, the challenges of implementation of IPE and, its impact on outcomes. **Methods:** A comprehensive review of the literature from 2005 to 2024 was conducted using PubMed, Google Scholar, and Scopus. Studies focusing on the role of IPE in patient care and teamwork were included. Non-peer-reviewed articles were excluded. **Results:** IPE improves clinical outcomes by improving communication, role clarity, and shared decision-making in orthopaedic teams. Effective strategies such as case-based learning and simulation training strengthen collaborative skills. Despite challenges such as time constraints and institutional resistance, customised training and curriculum integration provide viable solutions. **Conclusions:** Incorporating IPE into orthopaedic education is critical to promote teamwork and improve patient outcomes. Addressing challenges and fostering collaboration can drive innovation in orthopaedic care and enhance healthcare delivery around the world.

Keywords: Interprofessional Education, Orthopaedic, Collaborative Practice, Teaching Strategies, Healthcare

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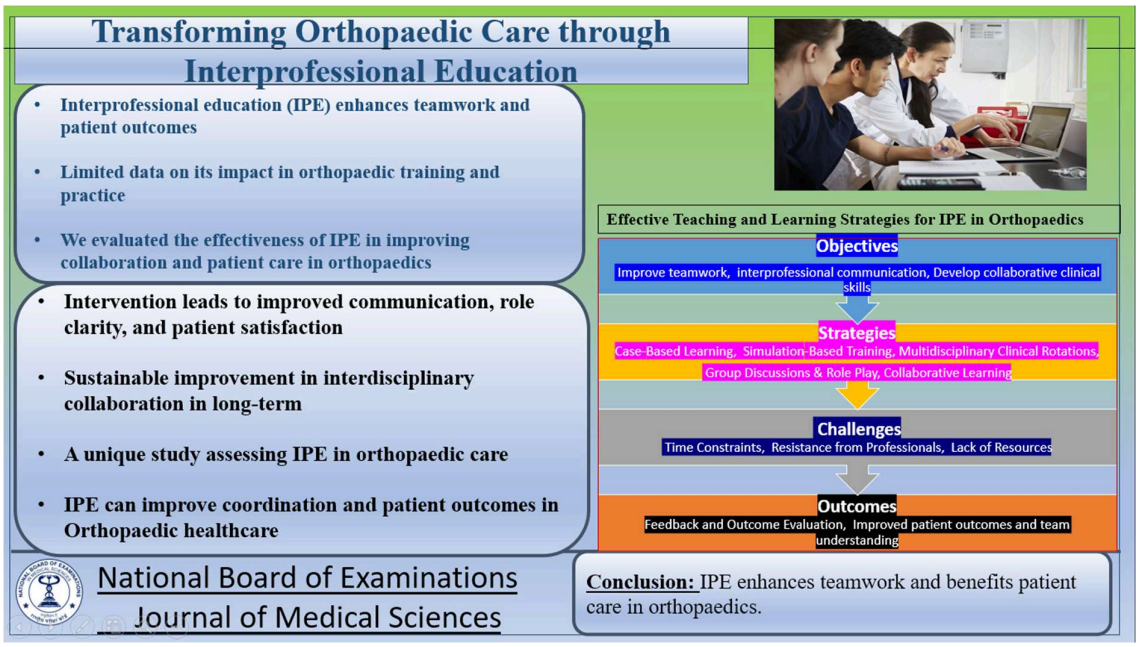
Graphical Abstract



Key Highlights

- Interprofessional Education (IPE) significantly improves clinical outcomes by fostering effective communication and collaboration among diverse healthcare professionals in Orthopaedics.
- The role of the core principles of the IPEC framework – ethics, roles, communication, and teamwork – in making interprofessional education (IPE) effective.
- Case-based learning, simulation-based training, and multidisciplinary clinical rotations are highlighted as key strategies that enhance teamwork and clinical skills among Orthopaedic professionals.
- The review identifies common barriers to IPE implementation, such as time constraints and institutional resistance, and proposes practical solutions to overcome these obstacles.
- Integrating IPE into residency programs can promote innovation in orthopaedic research and practice worldwide, leading to improved healthcare delivery.

1. Introduction

The World Health Organization (WHO) defines interprofessional education (IEP) as an experience in which "students from two or more disciplines learn from each other, from each other and from each other and facilitate each other to collaborate health outcomes" [1]. IEP improves patient care, by implementing multidisciplinary approach in orthopaedic care involving Orthopaedic surgeon, nurses, physician, physical therapists, anaesthesiologists, occupational therapists and other allied health professionals according to need of customised patient care [3]. The framework of interprofessional collaboration, focused on values, ethics, responsibilities, communication and teamwork [1,4]. Multidisciplinary interactions is crucial from preoperative planning, few important intraoperative decisions making as well as

during postoperative care and follow ups [5]. Therefore by strengthening team-based care and encouraging shared decision-making, interprofessional collaboration reduces medical errors, and improves outcome and satisfaction of patient [2,6]. IPE also prepares professionals to manage the dynamic clinical challenges by developing certain skills by other speciality of the teammates and resolve common conflict and confusion [7]. common Orthopaedic ailments which needs arthroplasty, arthroscopy and polytrauma or fracture management greatly benefit from these collaborative approaches [8,9]. This manuscript aims to review IPE delivery models in Orthopaedics, explores strategies to overcome obstacles in implementing, evaluating their impact on current and future patient care, and to know the the importance of shared learning of different disciplines.

2. Materials and Methods

- Search Strategy and Data Collection: A literature review was conducted using PubMed, Google Scholar and Scopus database to retrieve relevant articles published between 2005 to 2024. The keywords used in the search were “interdisciplinary education”, “orthopaedics”, “multidisciplinary teams”, “teamwork in health care”, “orthopaedic education”, “clinical collaboration” and “IPE in orthopaedics”.
- Inclusion and exclusion criteria: Studies focused on the integration of IPE in orthopaedics, its impact on patient care or its role in improving collaborative practice in the orthopaedic setting were included. Studies that did not involve IPE in healthcare or orthopaedic contexts or were not peer reviewed were excluded.
- Data synthesis: Data from those articles which were included, were analysed and classified according to themes, noting benefits of IPE, teaching and learning strategies, barriers to implementation and success. Studies bearing on the use of IPE in different subspecialities of orthopaedic specialties viz. trauma, geriatric orthopaedics, pediatric orthopaedics were retrieved, reviewed to assess their impact in the orthopaedic care.
- IPEC (Interprofessional Collaborative Education) framework analysis: It helps to explore the role of key IPE competencies of different studies: values and ethics, roles and responsibilities, processed interprofessional communication and teamwork, and [1,10] The integration of these core competencies in different education programs of orthopaedic speciality and their effect on professional collaboration were analysed.
- Review methodology: To summarize the findings of the literature, a narrative review methodology was done. It also identifies gaps in available literature, effectiveness of IPE strategies and their effect on patient care and on clinical practice. qualitative and quantitative data, educational assessments, and surveys on IPE effectiveness, including different types of articles, were assessed

3. Results and Discussion

3.1 Technology Integration

This section explores how telemedicine, AI-based tools, and simulation-based training are used in orthopaedics to improve teamwork and shared learning. How these technologies help health care professionals collaborate more effectively and improve patient care.

3.2 Comparison of IPE, Multidisciplinary, Interdisciplinary, and Transdisciplinary Approaches

Although IPE approaches, multidisciplinary, interdisciplinary, and intradisciplinary, all promote teamwork, they differ in how professionals engage and work with professionals of other speciality [11,12]. IPE focuses on collaborative learning to improve collaboration while multidisciplinary approach allow them to work separately so everyone solves their own problems [1]. In contrast, the Interdisciplinary approach combines expertise and perspectives to create integrated solutions [13]. The Transdisciplinary approach goes further by blending roles and expertise to address complex issues holistically [14]. Each approach has its merits and challenges, but they all aim to improve communication, understanding, and outcomes by leveraging the strengths of various professions (Table 1) [15,16].

Table 1. Comparison of IPE, Multidisciplinary, Interdisciplinary, and Transdisciplinary Approaches [11-18]

Aspect	Interprofessional Education (IPE)	Multidisciplinary Approach	Interdisciplinary Approach	Transdisciplinary Approach
Definition	Educating professionals from different disciplines to learn about, from, and with each other.	Professionals from different disciplines work on separate parts of a task or project without much interaction.	Professionals integrate their expertise and collaborate closely to develop shared solutions.	Professionals transcend disciplinary boundaries, working seamlessly to address complex, multifaceted problems.
Purpose	Foster collaboration, teamwork, and communication for better patient and professional outcomes.	Utilize individual expertise from each discipline to achieve a common goal.	Combine and synthesize knowledge for holistic problem-solving.	Create innovative solutions by blending disciplinary knowledge and roles, often leading to new perspectives and approaches.
Interaction	High: mutual learning and shared goals.	Minimal: limited interaction; each discipline works independently.	High: continuous communication and shared decision-making among team members.	Very high: roles and boundaries blur as professionals work together seamlessly.

Focus	Collaborative skills development and understanding roles.	Task completion within distinct disciplinary boundaries.	Integration of knowledge and collaborative problem-solving for comprehensive solutions.	Holistic, boundary-crossing approaches to solve complex, real-world problems.
Outcome	Improved teamwork and patient outcomes.	Achievement of discipline-specific tasks without full integration.	Innovation and holistic solutions with better outcomes through integrated efforts.	Groundbreaking solutions that transcend traditional boundaries and create new knowledge.
Example	Healthcare teams learning together to manage patient care collaboratively.	Cancer treatment teams where each specialist works independently on different aspects of treatment.	A team of surgeons, physiotherapists, and social workers jointly creating a rehabilitation plan.	A community health project where professionals from Healthcarehealthcare, engineering, and social sciences work together to solve health issues.

3.3. Core Objectives of Interprofessional Education (IPE) in Orthopaedics

The core objectives of IPE in Orthopaedics focus on enhancing teamwork, improving patient outcomes, and fostering respect across disciplines [1,7,19]. IPE ensures a holistic, patient-centered approach to orthopaedic care by promoting collaboration among healthcare providers (Table 2) [2,20].

Table 2. Core Objectives of IPE in Orthopaedics [1,2,7,15,16, 19,20,21]

Objective	Description	Strategies	Benefits	Core Competency Domains
Enhancing Collaborative Skills	Develops effective communication and teamwork among healthcare providers.	Cross-disciplinary training, role clarification	Improved decision-making, seamless care coordination	Roles & Responsibilities, Communication
Improving Patient Outcomes	Focuses on optimizing care to achieve better functional recovery.	Integrated care plans, shared patient management	Reduced complications, faster recovery	Team-Based Care, Values & Ethics
Building Mutual Respect Across Disciplines	Fosters understanding and respect for each healthcare professional's expertise.	Team-building exercises, mutual feedback	Enhanced collaboration, improved morale	Values & Ethics, Communication

In orthopaedic care, various healthcare professionals work collaboratively to ensure effective diagnosis, treatment, and rehabilitation for patients.[22] Each professional plays a unique and vital role, from diagnosis and surgery to post-operative care, rehabilitation, and psychosocial support.[23] Their coordinated efforts lead to better patient outcomes, improved recovery, and enhanced quality of life [24] (Table 3).

Table 3. Roles of Healthcare Professionals in Orthopaedic Care [22-30]

Healthcare Professional	Primary Responsibilities	Key Functions	Skills Required	Patient Interaction	Outcome Impact
Orthopaedic Surgeons	Diagnose and treat musculoskeletal issues. Perform surgeries.	Joint replacements, fracture repairs, treatment plans.	Surgical skills, musculoskeletal knowledge	Explain procedures, manage expectations.	Improves mobility, reduces pain.
Anaesthesiologists	Administer anesthesia, monitor vital signs during surgery. Manage post-operative pain.	Anesthesia management, post-operative care.	Expertise in anesthesia, risk assessment.	Ensure comfort during surgery, address concerns.	Reduces perioperative complications, ensures recovery.
Physiotherapists	Restore movement and function through exercises. Help with mobility and pain management.	Personalized rehabilitation programs, strength assessments.	Physical therapy knowledge, biomechanics expertise.	Guide rehabilitation, educate on injury prevention.	Speeds recovery, increases strength, prevents future injury.
Occupational Therapists	Help patients regain independence in daily activities. Adapt environments, provide assistive devices.	Assist with daily living activities, adaptive strategies.	Knowledge of daily living skills, ergonomic practices.	Help patients with tasks like dressing, cooking.	Enhances independence, reduces dependency.
Nurses	Monitor patients, manage pain, provide post-	Vital signs monitoring, medication administrati	Clinical care, patient education,	Offer reassurance, ensure recovery	Speeds recovery, reduces

	operative care, and educate on recovery.	on, wound care.	communication.	compliance.	complications.
Radiology Technicians	Perform imaging tests like X-rays and MRIs for diagnosis.	Diagnostic imaging for treatment planning.	Imaging technology expertise, attention to detail.	Ensure proper positioning for scans, explain the process.	Improves diagnostic accuracy, aids surgery planning.
Social Workers & Psychologists	Address emotional, social, and mental health aspects of injury or surgery. Provide counselling.	Emotional support, coping strategies, patient and family counselling.	Mental health expertise, counselling skills.	Provide one-on-one or family counselling.	Reduces anxiety, improves adherence to treatment plans.

IPE is vital in ensuring high-quality care in various Orthopaedic subfields [1,31]. By promoting collaboration between professionals from diverse disciplines, IPE enhances the patient experience and outcomes, particularly in complex care scenarios such as trauma, geriatric care, pediatric care, Orthopaedic oncology, and post-surgical rehabilitation [32]. Each area benefits from a multidimensional approach where team members work together to address all aspects of a patient's condition, from diagnosis and treatment to rehabilitation and psychosocial support.[17,33]

3.4 Applications of IPE in Orthopaedics

IPE in orthopaedics enhances patient care by fostering collaboration among healthcare professionals [1,34]. It ensures cohesive treatment strategies across trauma care, rehabilitation, geriatric management, pediatric orthopaedics, and oncology [35]. IPE integrates expertise to address complex patient needs, improve outcomes, and optimize recovery [32,35] (Table 4).

Table 4. Enhanced Applications of IPE in Orthopaedics [1,32,34-42]

Application Area	IPE Team Composition	Core Benefits	Notable Strategies
Trauma and Emergency Care	Trauma surgeons, anaesthesiologists, emergency personnel, radiologists, nurses	Faster interventions, reduced errors, enhanced survival rates	Hands-on clinical workshops, scenario-based training
Post-Surgical Rehabilitation	Orthopaedic surgeons, physiotherapists, occupational therapists, nurses	Optimized mobility, pain management, shorter hospital stays	Personalized rehab programs, interprofessional communication training

Geriatric Orthopaedics	Geriatricians, Orthopaedic surgeons, physiotherapists, social workers	Holistic care, improved quality of life, reduced complications	Integration of GERIATRIC 5Ms framework, multidisciplinary case reviews
Pediatric Orthopaedics	Paediatricians, Orthopaedic surgeons, physiotherapists, psychologists, social workers	Tailored care plans, developmental and emotional support, enhanced recovery	Anatomy demonstrations, collaborative functional assessments
Orthopaedic Oncology	Orthopaedic surgeons, oncologists, radiologists, physiotherapists, social workers	Comprehensive treatment, psychosocial support, long-term follow-up	Problem-based learning, community-based experiences
Educational Initiatives	Medical educators, clinical specialists, anatomists, physiotherapists	Improved collaboration and communication among students	Anatomy prosections, interprofessional workshops on MSK care
Research & Development	Healthcare researchers, Orthopaedic educators, medical students	Better preparedness for teamwork, improved patient outcomes	Interprofessional training wards, joint clinical studies
Cost Optimization	Administrators, Orthopaedic surgeons, financial officers	Reduced treatment costs, shorter recovery periods	Interdisciplinary budgeting sessions, implementation of cost-effective care pathways

GERIATRIC 5*M*s: Mind (Cognition and Mental Health), Mobility (Function and Physical Activity), Medications (Appropriate Prescriptions), Multicomplexity (Chronic Conditions), Matters Most (Aligning Care with Patient Goals).

3.5 Teaching and Learning Strategies for IPE in Orthopaedics

IPE in Orthopaedics is essential for promoting effective teamwork and enhancing patient care [1,7,43]. The first step is identifying learning objectives, such as improving teamwork, enhancing interprofessional communication, and developing collaborative clinical skills [44]. Once these objectives are set, the next step is to select teaching strategies, including case-based learning, simulation-based training, and multidisciplinary clinical rotations [45,46]. These strategies are then implemented through group discussions, role play, and collaborative learning platforms, fostering real-world clinical problem-solving [31,47]. Challenges like time constraints, resistance from professionals, and a lack of resources are addressed with practical solutions, including flexible scheduling, education on the value of IPE, and the use of technology [48,49]. Finally, outcomes are assessed through feedback mechanisms and evaluations, aiming for improved patient outcomes, enhanced understanding of team roles, and better preparedness for real-world clinical settings [7,50] (Figure 1).

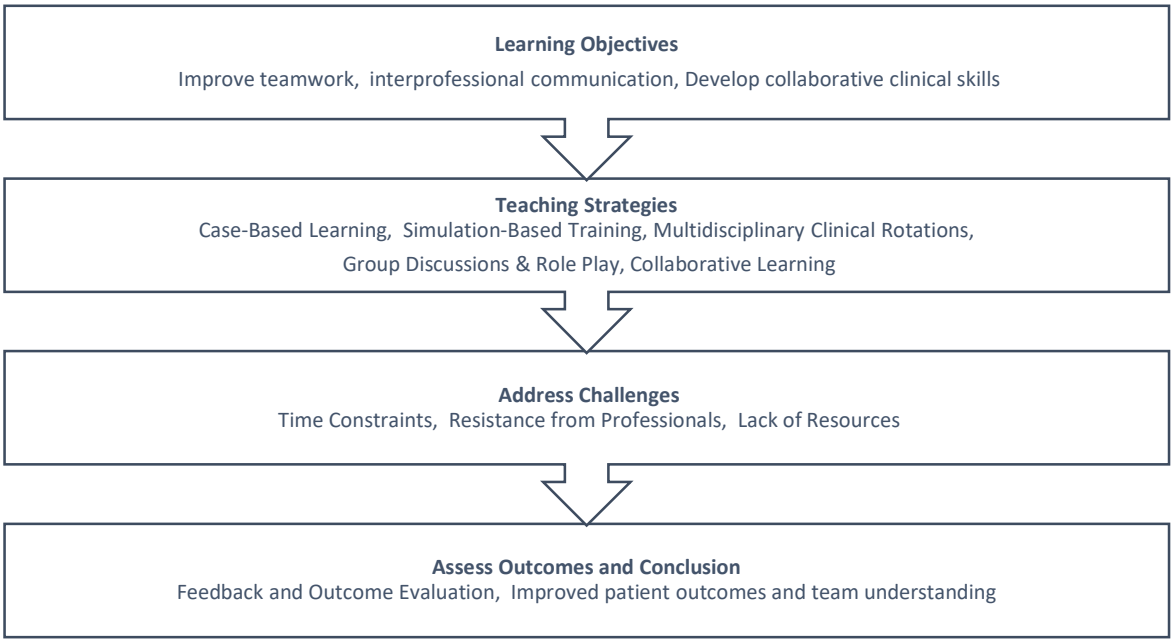


Figure 1. Effective Teaching and Learning Strategies for IPE in Orthopaedics [1,7,43-50]

These strategies facilitate the development of competencies required for effective interprofessional collaboration, improving overall patient outcomes in Orthopaedic care [32].

IPE in Healthcare focuses on fostering effective collaboration among various healthcare professionals to improve patient care. [1,7] By integrating different disciplines, IPE aims to enhance the quality of education and strengthen teamwork, enabling a holistic approach to patient treatment [31]. With the evolving healthcare needs, strategies like telemedicine, AI-driven planning tools, and simulation labs are essential to support the development of skills and competencies in collaborative practice [45,51] (Table 5).

Table 5: Strategies for Technology in IPE [45,51-55]

Strategy	Description	Impact on Orthopaedics
Telemedicine and Virtual Case Discussions	Use of digital communication tools to facilitate remote consultations and collaborative decision-making.	Enhances accessibility to expert consultations, enabling Orthopaedic surgeons to collaborate on complex cases, especially in rural or underserved areas. Facilitates learning across geographic boundaries, improving knowledge sharing and patient care.
AI-Driven Orthopaedic Planning Tools	Incorporating artificial intelligence into surgical planning and diagnostics to assist in decision-making.	AI tools can help orthopaedic surgeons predict surgical outcomes, plan complex surgeries, and improve treatment precision. This enables more personalized patient care and enhances learning about various treatment strategies.

Role of 3D Printing in IPE	Utilizing 3D printing technology for creating anatomical models, prosthetics, or surgical tools.	3D printing helps Orthopaedic surgeons, physical therapists, and other healthcare professionals visualize anatomical structures in greater detail, enhancing surgical planning, patient education, and rehabilitation.
Simulation Labs for Surgical Training	Virtual and physical simulation labs allow healthcare providers to practice surgeries and procedures in a controlled, risk-free environment.	Simulation-based training improves surgical skills by providing hands-on experience, reduces errors, and fosters teamwork. It supports interprofessional learning by allowing various healthcare providers, including surgeons, anaesthesiologists, and nurses, to practice together, improving collaborative care in real-world scenarios.

These strategies represent how technology is shaping the future of interprofessional education in Orthopaedics, enhancing the collaborative learning environment and improving patient outcomes.

3.6 Challenges and Controversies in Implementing IPE

While IPE in Orthopaedics aims to improve collaborative care and enhance patient outcomes, its implementation faces several challenges and controversial points [2,20]. These include issues such as the resistance to change within traditional educational systems, disparities in institutional support, and the effectiveness of IPE models [48,56]. There is also ongoing debate regarding how best to assess the outcomes of IPE and whether the expected benefits truly justify the resources invested in such programs [34]. Below is a comprehensive table outlining these challenges, possible causes, proposed solutions, and the impact on learning outcomes (Table 6).

Table 6. Challenges, Causes, Solutions, and Impact on Learning in Implementing IPE in Orthopaedics [1,2,7,19,57-63]

Challenge	Description	Possible Causes	Solutions	Impact on Learning
Resistance to Change	Reluctance to adopt new educational approaches.	Deeply ingrained traditional practices and a lack of understanding of IPE's benefits.	Implement pilot programs, showcase successful outcomes, and integrate IPE into curricula.	Facilitates a shift towards collaborative learning.
Logistical & Financial Barriers	Insufficient resources to support IPE initiatives.	Budget constraints, lack of shared spaces (e.g., simulation labs).	Allocate dedicated time, invest in shared facilities, seek external funding.	Enables smooth operation and sustainability of IPE programs.

Cultural Challenges	Differences in professional attitudes and perceptions.	Stereotypes, professional silos, resistance to new practices.	Promote team-building activities, clear role definitions, respect for diverse viewpoints.	Improves collaboration and respect across professions.
Curriculum Constraints	Overcrowded curricula and limited time.	Overloaded schedules, competing priorities.	Create interprofessional time slots, use online platforms for asynchronous learning.	Allows room for IPE integration in academic calendars.
Accreditation & Standards	Lack of clear IPE accreditation guidelines and standards.	Varying institutional policies and accreditation bodies.	Develop institutional policies, advocate for accreditation standards.	Ensures formal integration of IPE into educational standards.
Inadequate Faculty Preparation	Lack of faculty training for interprofessional teaching.	Traditional faculty training, lack of interprofessional expertise.	Offer faculty development programs focused on IPE teaching skills.	Enhances the quality of IPE instruction.
Measurement of Outcomes	Difficulty in assessing IPE effectiveness.	Lack of standardized metrics or outcomes.	Develop evaluation frameworks, collect feedback, assess student outcomes.	Provides data to refine and improve IPE programs.
Students' Resistance	Students' reluctance to engage in IPE.	Lack of familiarity with collaborative practice, perceived irrelevance.	Offer real-world case scenarios, foster peer learning, highlight IPE's career value.	Increases student engagement and participation.
Institutional Support	Lack of institutional backing for IPE.	Leadership not prioritizing IPE, competing institutional priorities.	Secure leadership support, ensure funding, embed IPE in institutional mission.	Encourages long-term institutional commitment to IPE.

3.7 Controversies in IPE Implementation

While many advocates of IPE argue for its efficacy in improving healthcare delivery, some critics question whether the outcomes justify the cost and resource allocation, especially in lower-resource settings [64]. Some stakeholders argue that integrating IPE into an already packed curriculum may dilute the focus on essential Orthopaedic skills. Others believe

it enhances clinical practice by fostering collaborative skills [1,7]. The lack of universally accepted, standardized measures for assessing IPE effectiveness remains contentious. There is a debate on how to quantify best improvements in patient care, team dynamics, and professional development [32]. The degree of support from academic institutions varies widely. While some institutions prioritize IPE, others remain hesitant, citing concerns over its long-term sustainability and alignment with other educational goals [65].

IPE can be integrated into educational programs by addressing these challenges and controversies through targeted solutions and ongoing dialogue, fostering collaborative practice and improving healthcare outcomes.

3.8 Evaluation and Accreditation of Interprofessional Education (IPE) in Orthopaedics

The evaluation and accreditation of IPE programs play a critical role in ensuring their effectiveness and sustainability within Orthopaedic education [1]. Accreditation bodies set clear goal to maintain high standards, to improve quality of team work and collaboration among healthcare professionals [1,66]. Evaluation of IPE programs means assessing at learning outcomes, Behavior changes, and improvements in patient care, aiming to better healthcare delivery [67]. Real clinical settings help measure the effectiveness of healthcare teams [68]. It also identify areas for improvement, and ensure that IPE remains relevant and effective [1,7,31]. This section discusses the metrics used to measure the success of IPE programs, the role of accreditation bodies in promoting these programs, and the tools employed to assess interprofessional collaboration, focusing on their specific application in Orthopaedic education [1,64]. The following table concisely overviews these key elements (Table 7).

Table 7. Key Elements in the Evaluation, Accreditation, and Assessment of IPE Programs in Orthopaedic Education [1,20,32,60.69-71]

Subsection	Key Points	Tools/Methods	Impact on Orthopaedic Education
Metrics for Success in IPE Programs	- **Learning Outcomes**: Assess knowledge and skills before and after IPE. - **Behavioural Change**: Monitor improvements in teamwork and communication. - **Patient Outcomes**: Track clinical improvements and patient satisfaction. - **Feedback**: Gather input from learners and faculty.	- Pre- and post-program assessments. - Competency frameworks (e.g., ICCAS). - Patient outcome tracking.	- Aligns education with real-world Orthopaedic practice. - Supports data-driven refinement of IPE.
Role of Accreditation	- **Standards**: Set quality criteria for IPE programs. -	- Accreditation standards. - Re-	- Ensures high-quality, sustainable

Bodies in Promoting IPE	**Recognition**: Ensure credibility and institutional support. - **Continuous Improvement**: Promote regular program updates. - **Multidisciplinary Involvement**: Encourage collaboration across professions.	accreditation processes.	IPE in Orthopaedics. - Promotes interprofessional engagement in education.
Tools for Assessing Interprofessional Collaboration	- **Competency Tools**: Evaluate communication and teamwork skills. - **Readiness Scales**: Measure attitudes towards collaboration. - **Team Performance Tools**: Assessing collaboration of healthcare professional in real time clinical setting. - **Patient-Centered Metrics**: Assess collaboration through patient outcomes.	- ICCAS, RIPLS, real-time observation tools. - Patient satisfaction surveys.	- Enhances collaboration within Orthopaedic teams. - Improves patient care through better team dynamics.

ICCAS: Interprofessional Collaborative Competency Attainment Survey, RIPLS: Readiness for Interprofessional Learning Scale

3.9 Global Perspectives on IPE in Orthopaedics

Inter professional education is an essential part of healthcare training in almost all part of the world. it helps professionals involved in orthopaedic care in various ways. it improves patient care not only in developed world but also in developing countries with limited resources [2]. Different models of IPE were described based on different healthcare needs and difference in availability of resources. These models have one thing in common that they all promotes collaboration among health care professionals of different speciality and a culture of shared responsibility [72]. IPE proven to have a positive impact on Orthopaedic education, which varies in different parts of world based institutional, administrative, system-level processes and available resources [73]. A few IPE models, explores initiatives in low-resource settings, and international collaboration to improve healthcare by means of improving patient care and Orthopaedic education [1].

3.9.1 IPE Models in Developed Countries

IPE in developed world with the adequate resources and takes full advantage of advanced infrastructure, modern technology, and multidisciplinary collaboration [1,73]. IPE in these settings are often quite clear with guidelines for student interaction, shared decision, role definition, and collaborative practice competencies [1,7,74]. Adequate resource models focus on improving clinical and communication skills among different medical subspeciality, nursing, physiotherapy, and other allied health students. It aims to improve patient

outcomes through teamwork. Various assessment tools were used by an institution to ensure quality patient care and education by means of collaborative practice in real-world Orthopaedic settings [1,7].

Mohammed (2021) explains about collaboration among different professionals improves both healthcare delivery as well as quality of education [1]. While describing importance of IPE framework, the importance of synergy between healthcare education and practice by regulatory and accreditation bodies in developed countries were explained. Which is crucial to ensure latest advancements in clinical care and teamwork by updating IPE programs time to time [7,76].

3.9.2 IPE Initiatives in Low-Resource Settings

Challenges in implementing traditional IPE models, includes limited resources in terms of educational materials, faculty, and clinical setting [48,57]. However, various IPE initiatives have emerged in such constrained situation and local need can that adapt modified IPE model keeping in mind about local healthcare need.[77] Innovative solutions such as telemedicine, online learning platforms, helps to reduce financial burden. Collaboration between local institutions also help to adopt IPE model satisfactorily with such limited resource settings. The focus on these IPE programs is basically on the essential competencies, such as patient based care, communication, and team coordination [2,78].

Khalili (2024) explains that collaborative partnerships are essential to develop effective IPE programs, helps in overcome institutional barriers in low-resource settings [63]. Thus improving interprofessional collaboration is essence of such IPE program to enhances the quality of Orthopaedic care in limited resource settings [79].

3.9.3 International Collaboration in Orthopaedic Education

Different institution collaboration beyond borders in terms of sharing Orthopaedic skills, education, resources, benefits both developed and low-resource settings equally [80]. These collaborations by means of exchange knowledge, developing training programs, and multicentric research initiatives aimed at improve quality of health care and competencies of specialist including Orthopaedic surgeon. These collaborations help to perform IPE program in more standard way in different settings. [1,34]

As health challenges are different in different parts of the world in different time zones, international collaboration in IPE also helps in sharing such problems which happens in one part of world and expected to be problem in other part. This allows healthcare professionals to learn together and learn from one another, to integrate such knowledge in clinical practices, research and future innovation. The exchange of clinical as well as surgical skills, mutual understanding integrate in the development of IPE programs and based on evolving health needs in Orthopaedics speciality [11].

3.10 IPE in Research and Innovation in Orthopaedics

Advanced research and innovation in Orthopaedics is better if collaboration between different speciality among health professionals to develop integrated approach, guidelines to follow, new management techniques, devices, and strategies [1,2]. Research focused on

integration of diverse perspectives of healthcare, taking care of local health needs lead to better healthcare, even with limited resources and helps to develop guidelines for other such health centers [2]. Innovations are essential, not only for research, but also to accelerate the development of personalized treatments and quality care at grassroot label and within reach of healthcare institution of developing countries [81]. Collaborative efforts helps particularly in developing new technologies, implants, orthotic and prosthetic devices, and conducting, multidisciplinary clinical trials [82].

3.10.1 Collaborative Research on Implants and Techniques

Orthopaedic implants design and newer innovation of implants is benefitted immensely from IPE [34]. 3D and 4D printing technologies have revolutionized the innovation of newer and better implants. Thus patient-specific implants and more precise implants according to different age, sexes and anatomical position are taken into consideration during the innovation [83]. Biomedical engineers, and material scientists in collaboration with Orthopaedic surgeons, are able to create creation more specific and durable implants that improve outcomes with much less complication due to implant and minimize recovery times [84]. Robotics, custom-made implants and rapid development of prototyping techniques, helps to orthopaedic surgeon in simplifying complex surgery to some extent [85].

3.10.2 Development of New Orthotic and Prosthetic Devices

IPE collaborative teams involving prosthetists, engineers, and rehabilitation experts in addition to Orthopaedic surgeon work together to develop newer and more efficient **Orthotic and Prosthetic Devices** for better, comfort, and patient satisfaction [87]. Addition of 3D printing, enable better customization of these devices according to individual patient needs [88]. 4D printing technology is still emerging and offers better adaptability of these devices with better response to environmental stimuli, and overall patient satisfaction [83].

3.10.3 Multidisciplinary Clinical Trials in Orthopaedics

Integration of IPE in designing as well as in execution of multidisciplinary clinical trials that evaluate interventions, surgical technique to rehabilitation are significant [82]. It involves collaboration between different specialities viz surgeons, physician physiotherapists, radiologists, and rehabilitation specialists [32]. This approach involves in preoperative, intraoperative as well as postoperative rehabilitation, which lead to more effective management protocols [89]. Thus IPE enhances the preparedness as well as effectiveness of clinical trials, to produce more reliable findings intern benefit different groups of patients [34].

3.11 Future Directions in IPE for Orthopaedics

IPE ensures teamwork, better health services and ensure collaboration of different medical speciality effectively in complex clinical settings [1,31]. The future of IPE needs to address emerging challenges in Orthopaedic care especially in rural set ups, during training program such as residency and fellowship programs, aiming to better healthcare, and knowledge sharing worldwide.[90]

3.11.1 Expanding IPE to Rural and Remote Care Settings

One of the most promising directions for IPE in Orthopaedics is its expansion into rural and remote care settings [91]. As the World Health Organization (WHO) emphasizes, work-based IPE has the potential to modify practices and improve patient care, particularly in underserved regions where resources are often limited [7]. By incorporating IPE into rural healthcare delivery, Orthopaedic teams can leverage collaborative skills and share expertise to overcome the shortage of specialists [34]. Integrating IPE into the existing healthcare frameworks rather than offering it as a separate course, as highlighted by the National Institutes of Health (NIH), ensures a more sustainable and viable approach [1,92]. This allows healthcare professionals in rural areas to enhance their competencies in collaborative care, improving patient outcomes even in resource-constrained environments [93].

3.11.2 Integrating IPE into Residency and Fellowship Programs

Integration of IPE during fellowships as well as residency is essential helps in for shaping future collaborative practice as well as to keep future Orthopaedic professional updated in clinical skills [1,7,34]. It also helps to understand the roles and contributions of different healthcare professionals [31]. Such integration promotes teamwork and patient specific care [94]. It also helps Orthopaedic trainees to better prepared for multidisciplinary work, even when there is scarcity of other speciality in the institution. Trainees will able to collaborate more effectively with other health professionals in their parent institution after completion of the course [1,19]. Thus, understanding the role as a team player also helps in better judgement in the clinical setting and improved outcomes in complex cases [15].

3.11.3 Role of IPE in Value-Based Orthopaedic Care

Value-based care is another aspect in shaping the future of IPE in orthopaedics. This approach prioritizes patient outcomes, cost-effectiveness, and satisfaction. Goals are best achieved through teamwork [21]. IPE helps healthcare providers collaborate to create efficient, patient-centered treatment plans and guidelines. By improving communication and coordination, it ensures high-quality care while making the best use of resources [1,2]. Research shows that integrating IPE into healthcare teams improves patient experiences and improves clinical outcomes, making it a vital part of modern orthopaedic care [79].

3.11.4 Global Networking and Knowledge Sharing

Global collaboration and knowledge sharing are essential to the future of IPE in orthopaedics. Working across borders helps improve healthcare around the world [1,34]. Through international collaboration, professionals can share research, clinical experience, and new treatment approaches [95]. This exchange of ideas and the latest advances in orthopaedic care are the key roles IPE plays. It bridges knowledge gaps and promotes shared learning across different healthcare systems [1,7]. Ultimately, a strong global network ensures that new techniques, treatments, and care models reach patients everywhere.

3.12 Limitations

This review has some limitations, which includes bias during literature search, as relying on specific databases and keywords may miss relevant studies in less accessible journals and publications of other language. Only published research is taken into consideration, but real-world experiences of clinical settings of developing world, which remain unpublished are not included. Differences in methodology across studies is another obstacle to draw broad conclusions. The review primarily considers healthcare professionals' perspectives, with less focus on patient experiences, which are essential for a full understanding of the impact of IPE. While implementation challenges are discussed, the institutional barriers of different healthcare settings may not be fully addressed. More research of current timeline is needed to evaluate how IPE strategies work in different orthopaedic environments.

Conclusion

IPE helps healthcare professionals in Orthopaedics speciality to work better needs working together. By improving communication, defining roles, and encouraging shared decision-making, IPE leads to improved patient outcomes. Practical teaching methods such as case-based learning and simulation training helps in building strong teamwork skills. While there are challenges to implement IPE, practical solutions can make it easier to adopt in clinical settings. Strengthening collaboration through IPE can transform orthopaedic education and practice, improving patient care worldwide.

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Conflict of Interest

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Author's Contribution

JSB: Conceptualization, Data Analysis, Literature Search, Manuscript writing, editing and final approval; RV: Conceptualization, Data Curation and Analysis, Literature Search, Manuscript writing, editing and final approval; JM: Conceptualization, Manuscript editing, and final approval;

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ORIGINAL ARTICLE

Profile of Road Traffic Accident Cases Autopsied at ACSR Government Medical College, Nellore, in 2022: A Retrospective Study

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Abstract

Road traffic accidents (RTAs) are a major cause of death and disability in low- and middle-income countries, contributing significantly to the global burden of disease. The primary causes of RTAs include over speeding, inappropriate driving, and poor road conditions in India. This study, conducted at a tertiary healthcare hospital in Nellore city, Andhra Pradesh, aimed to profile fatal RTAs, identifying the leading causes of death and factors contributing to accidents. The major cause of death in road traffic accidents in this study was head injury. Males aged 21 and above, along with pedestrians and two-wheeler riders, were the most affected groups. Preventing these fatalities requires a coordinated effort between civic authorities, police, and first responders to reduce pre-hospital deaths. Road safety awareness, along with improvements in infrastructure and traffic management, are essential to reducing the incidence and severity of these accidents in Nellore city.

Keywords: Road traffic accident, Traffic medicine, Cause of death, Autopsy, Mortality

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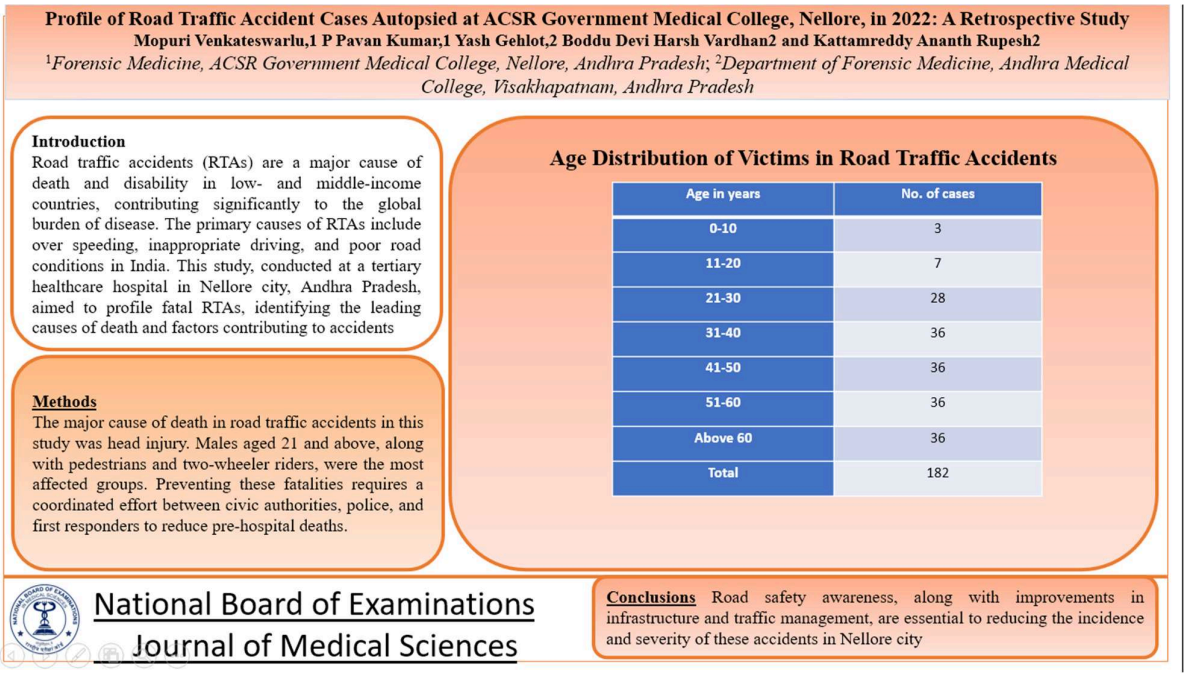
Graphical Abstract



Introduction

Road traffic accidents (RTAs) are among the leading causes of mortality and morbidity globally. They constitute a significant component of the global burden of disease and have garnered increasing attention within the field of public health [1]. RTAs result from a complex interplay of factors, which may be broadly categorized into human-related factors, vehicular factors, and external environmental variables. The important causal elements include speeding, driver error, influence of drugs/alcohol, distracted driving/mobile phone use, mechanical failure/ vehicular maintenance, suboptimal road conditions, poor visibility, adverse weather, failure of safety mechanisms such as airbags, and deficiencies in vehicle design to name a few.

Although the complete prevention of RTAs remains a formidable challenge due to the multifactorial nature of these events, mitigation of injury severity and reduction of fatalities represent achievable public health goals. This is principally relevant given that certain risk factors are modifiable and can be targeted through interventions. Comprehensive studies focusing on the determinants of RTAs and associated mortality are essential for designing interventions for prevention. A detailed analysis of the causes of death in RTAs provides significant insights into the effectiveness of current safety measures, including seat belts, helmets, and airbag deployment systems. Such research is vital to evaluate whether existing protective strategies are adequate or whether additional engineering/design modifications, legislative measures, or public health interventions are required to enhance occupant/pedestrian protection and reduce fatal outcomes in road traffic fatalities. Finally, with pedestrians being a major portion of RTA victims, a study on patterns of injuries and understanding the accident dynamics in pedestrians paves the way for designing walkways, elevated foot paths and planning urban infrastructure in a pedestrian-friendly manner [3].

Nellore city is the headquarters of Sri Potti Sriramulu Nellore district, located in the south coastal region of Andhra Pradesh. The present study aimed to analyze the profile of road traffic accident cases autopsied at the only tertiary health care facility in Nellore. The major objectives of the study were to assess the socio-demographic profile of the victims, evaluate the timing of accidents, identify the factors responsible for road traffic accidents, and examine the causes of death in different types of road traffic accidents [4]. This study complements the data available in the crime records and is a first step towards traffic medicine studies in the region. The study addresses the main research gap on understanding the factors like which type of injuries are causing major spot deaths, and the time during which accidents are more common in our region.

Methodology

This retrospective study included all road traffic accident cases autopsied at ACSR Government Medical College during the calendar year 2022. Data were collected from First Information Reports (FIRs), inquest reports, postmortem examination reports, toxicology reports i.e., chemical analysis of viscera reports, motor vehicle inspection reports and relevant medical records. RTA cases with incomplete data (final opinions pending or inaccessible files), along with all other cases, were excluded from the study. Descriptive statistical analysis of the data has been carried out by tabulating the variables in Microsoft Excel. A total of 182 RTA cases were included for analysis.

Results

The age distribution of victims of RTA is summarised in Table 1 with most victims being adults above the age of 21 years (172). Sex distribution of the victims is presented in Table 2 with males (142) being the large group of victims.

Table 1. Age Distribution of Victims in Road Traffic Accidents.

Age in years	No. of cases
0-10	3
11-20	7
21-30	28
31-40	36
41-50	36
51-60	36
Above 60	36
Total	182

Table 2. Sex Distribution of Victims in Road Traffic Accidents

Age Group	Gender		
	Female	Male	Total
0-10	3	0	3
11-20	1	6	7
21-30	1	27	28
31-40	5	31	36
41-50	6	30	36
51-60	9	27	36
61 Above	9	27	36
Total	**34**	**148**	**182**

The factors responsible for road traffic accidents in the victims are presented in Table 3. Over-speeding and driver negligence were identified as the major causative factors to the fatalities. While a few cases of hit and run were also noted [11].

Table 3. Factors Responsible for RTAs

Factor	Hospital death	Spot death	Total
Driver error (hit and run)	11	0	11
Drivers under the influence of alcohol	5	3	8
Overspeed	76	87	163
Total	92	90	182

The distribution of road traffic accidents across different times of the day shows that from 12 AM to 6 AM, there were 29 incidents, accounting for 15.93% of the total cases. Between 6 AM and 12 PM, 58 incidents occurred, making up 31.87% of the total. From 12 PM to 6 PM, there were 45 incidents, representing 24.73% of the total, while from 6 PM to 12 AM, 50 incidents were recorded, comprising 27.47% of the total.

The cause of death profile of the victims is tabulated in Table 4. The data shows that most fatalities were due to head injuries, with 65 deaths occurring at the hospital and 60 at the spot, totalling 125 cases.

Table 4. Cause of Death in RTA Victims

CAUSE OF DEATH			
	PLACE OF DEATH		
AGE GROUP	Hospital	Spot	Grand Total
0-10			
Head Injury	2	1	3
11-20			
Blunt Trauma to Abdomen	1	0	1
Head Injury	1	3	4
Multiple Injuries	1	1	2
21-30			
Blunt Trauma to Abdomen	1	0	1
Blunt Trauma to Chest	1	1	2
Head Injury	10	9	19
Multiple Injuries	1	2	3
Poly Trauma	2	1	3
31-40			
Blunt Trauma Chest and Abdomen	0	1	1
Blunt Trauma to Abdomen	1	1	2
Head Injury	14	10	24
Multiple Injuries	1	5	6
Poly Trauma	2	1	3
41-50			
Blunt Trauma to Abdomen	0	1	1
Crush Injury to Both Legs	1	1	2
Crush Injury to Leg	1	0	1
Head Injury	10	16	26
Multiple Injuries	5	0	5
Poly Trauma	0	1	1
51-60			
Blunt Trauma to Abdomen	0	2	2
Blunt Trauma to Chest	1	0	1
Crush Injury to Both Legs	1	0	1
Crush Injury to Leg	1	0	1
Head Injury	14	10	24
Multiple Injuries	2	3	5
Poly Trauma	1	1	2
61 Above			
Blunt Trauma to Abdomen	1	1	2
Head Injury	14	11	25

Multiple Injuries	2	2	4
Poly Trauma	2	3	5
Grand Total	**94**	**88**	**182**

The factors responsible for accidents in different vehicle types within the study population are summarized in Table 5, with two-wheeler accidents being the most common. The total number of victims in the study was 182 as mentioned earlier. The largest group of victims were two-wheeler users, with 88 riders and 20 pillion riders, totalling 108. This was followed by occupants of four-wheelers, including 14 rear occupants, 4 drivers, and 4 front-seat occupants, totalling 22. Pedestrians accounted for 52 victims.

Table 5. Vehicle Type and Factors Responsible for the RTA

AGE GROUP	FACTORS RESPONSIBLE FOR ACCIDENT			
TYPE OF VEHICLE	DRIVER ERROR (HIT AND RUN)	ALCOHOL INFLUENCE	OVER SPEED / DISTRACTED	GRAND TOTAL
0-10	0	0	3	3
2-Wheeler	0	0	3	3
11-20	1	1	5	7
2-Wheeler	0	1	5	6
4 Wheeler	1	0	0	1
21-30	2	1	25	28
2-Wheeler	0	1	20	21
3-Wheeler/Auto	0	0	1	1
4-Wheeler	2	0	2	4
Lorry	0	0	2	2
31-40	1	2	33	36
2-Wheeler	0	2	19	21
3-Wheeler /Auto	0	0	4	4
4-Wheeler	1	0	6	7
Bus	0	0	1	1
Lorry	0	0	2	2
Tractor	0	0	1	1
41-50		2	34	36
2-Wheeler	0	1	20	21
3-Wheeler Auto	0	0	1	1
4-Wheeler	0	0	8	8

Lorry	0	0	3	3
Mini Van	0	1	0	1
Tractor	0	0	1	1
Unknown Vehicle	0	0	1	1
51-60	3	2	31	36
2-Wheeler	1	2	14	17
3-Wheeler Auto	0	0	1	1
4-Wheeler	2	0	11	13
Lorry	0	0	3	3
Tractor	0	0	2	2
61 Above	4	0	32	36
2-Wheeler	2	0	16	18
3-Wheeler Auto	0	0	1	1
4-Wheeler	1	0	15	16
Unknown Vehicle	1	0	0	1
Total	11	8	163	182

Discussion

Road traffic accidents are a leading cause of unnatural deaths in developing countries, contributing significantly to injury-related disabilities and imposing a heavy socioeconomic burden. Despite these countries accounting for only 60% of the world's vehicles, they experience 93% of global road fatalities. The increasing number of road traffic deaths, driven by rapid urbanization and greater motorization, underscores the severity of this issue. Moreover, even in higher-income countries, individuals from lower socio-economic backgrounds are disproportionately affected by road traffic-related fatalities [5,6].

The present study reveals that males over 21 years of age are the most affected group in road traffic accidents, likely due to their active lifestyle, including commuting to work and other essential travel. Speeding is identified as the leading contributor to fatalities, with many deaths occurring at the scene of the accident. Head injuries are the primary cause of death, and two-wheeler riders are the most common victims, followed by pedestrians. Additionally, alcohol abuse is found to be a significant risk factor for road traffic accidents.

In a study by Sete et al. [7], the major cause of death was craniocerebral injury/head injury, with males being more frequently involved, is consistent with the findings of our study. But the higher number of spot deaths and pre-hospital care deaths in the present study indicate the fatal nature of the injuries and highlight the need for more timely medical attention. Global mortality of motorized 2–3 wheelers has increased by a relative ratio of 1.36 over a recent decade [8]. A similar trend of increased fatalities were noticed in terms of two-wheeler accidents in our study. Speeding, whether excessive or inappropriate, contributes to approximately 54% of global fatalities, with higher proportions observed in low- and middle-income countries (57%) compared to high-income countries (28%).

Our results show a similar trend, with over speeding identified as a major contributor to road traffic accidents [9].

The WHO has said that RTAs are the eight leading cause of death globally [10]. RTA autopsies constitute no less than a quarter of all unnatural deaths autopsied at our institute annually (the total annual autopsies conducted are around 800-1000). Although the present study indicates that 32% of road traffic accidents occurred between 6 AM and 12 PM, most accidents typically happen during the night hours, as seen in previous studies [11].

Interventions to prevent road traffic accidents (RTAs) include improving road safety infrastructure, enforcing stricter traffic laws, and promoting safe driving behaviours through public awareness campaigns. Additionally, measures such as implementing speed limits, enhancing vehicle safety features, and promoting the use of seat belts and helmets can significantly reduce fatalities. Targeted interventions in high-risk areas and for vulnerable road users, like pedestrians and motorcyclists, are crucial. Furthermore, effective emergency medical services and timely medical attention can help minimize the impact of injuries from RTAs [12].

In India, road safety has become a top priority, with the government adopting a comprehensive approach focused on education, engineering, enforcement, and emergency care. The new Motor Vehicles Act also imposes strict penalties for safety violations. Additionally, initiatives such as cashless treatment for accident victims and the installation of ambulances at toll plazas aim to reduce fatalities and improve response times [13].

A major limitation of the present study is the incomplete availability of data on the use of seat belts and helmets, which were therefore excluded from the analysis. However, these are important factors that could influence the outcomes of road traffic accidents.

Future studies of this sort are to be conducted annually in close collaboration with the district crime records bureau on all available datasets to identify key controllable variable in striving towards reducing the number of road traffic accident fatalities in Nellore region.

Conclusion

The present study on road traffic accidents in Nellore city during 2022 highlights that males aged 21 and above are most frequently involved, with two-wheeler riders and pedestrians being the primary victims. Over-speeding was identified as a key factor contributing to accidents. The high number of spot and pre-hospital deaths indicates the need for better coordination between civic authorities, the police, and hospitals for timely care. Promoting safety awareness, improving road infrastructure, and enhancing traffic management are essential to reducing fatalities and ensuring a safer city for all. Creating proper footpaths, walkways, and cycling tracks in Nellore city can encourage people to reduce their reliance on personal vehicles. Additionally, the lack of a robust public transport system and the excessive presence of three-wheeler autos contribute to the risk of road traffic accidents. Addressing these issues by improving infrastructure and promoting public transport would be key to reducing accidents and enhancing safety in the city.

Conflicts of interest

The authors declare that they do not have conflict of interest.

Ethics committee approval

The study has been approved by the Institutional Ethics Committee of ACSR Government Medical College, as per reference number 083/SRC/2024, dated 06/01/2025.

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ORIGINAL ARTICLE

Evolution and Current Trends in Bleomycin Therapy for Lymphangiomas: A Comprehensive Review and Future Directions

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Abstract

Background: Lymphangiomas are rare congenital malformations that and pose a specific challenge in the pediatric age group and require effective therapeutic intervention. In our systematic review we look at how bleomycin therapy for lymphangiomas has evolved across the five decades from (1977-2024). **Methods:** We conducted a systematic literature review of 127 studies, via a comprehensive search of a plethora of databases including PubMed/MEDLINE, Embase, and Cochrane Library. This analysis of studies allowed us to chart the gradual transition from surgery being the mainstay of treatment to bleomycin becoming a preferred treatment modality. **Results:** Analysis of our observations showed that our current success rates for bleomycin therapy range from 60-88%, with huge age dependent variations in the treatment responses. Protocol refinement has led to a significant improvement in standardization of therapy. Optimal concentration of 1 IU/mL with maximum cumulative therapy dose of 15 IU/kg are the established standards now. **Conclusions:** Recent advances in molecular pathophysiology have yielded promising results from combination therapy approaches which suggests new avenues for more efficacious treatment methods. We propose structured evidence based recommendations which emphasise the standardisation of protocols whilst incorporating personalized therapy based on lesion morphology and patient characteristics.

Keywords: Lymphangioma, Bleomycin, Sclerotherapy, Cystic Hygroma, Treatment Outcomes

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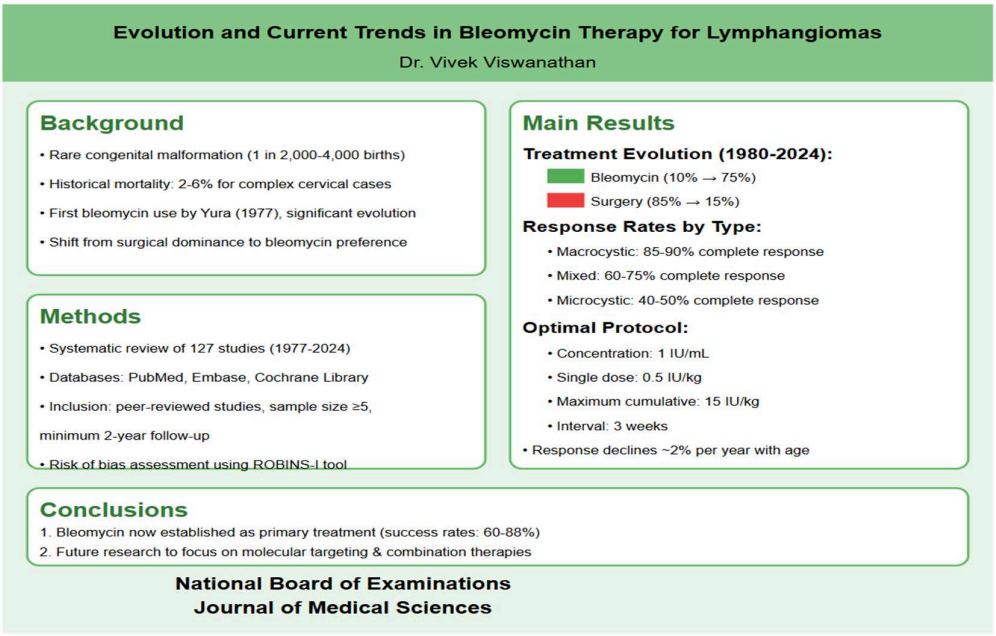
Graphical Abstract



Introduction

Lymphangiomas present a specific therapeutic challenge for pediatric patients. With an incidence of approximately 1 in 2,000-4,000 live births [1,2], these benign lymphatic malformations greatly impact the quality of life of children, particularly when these cases are situated in anatomically sensitive regions [3]. Historical mortality of complex cervical lymphangioma patients of 2-6% significantly highlights the importance of effective methods of treatment [4,5].

The use of bleomycin therapy in the treatment of lymphangiomas presents an interesting narrative of medical innovation. When Yura and colleagues first described the use of bleomycin as a sclerosant in 1977 [6], it was met with considerable skepticism by the medical community. Tanigawa's landmark study published a decade later provided the first systematic evidence of these changes. The results however varied greatly [7].

The early 1990s saw stiff debate between the Japanese school led by Hashimoto [8] that argued in favor of large doses of bleomycin being used for the management of lymphangiomas and European centers that favored higher than normal doses with frequent administration [9]. Recent advancements (post-2000), including imaging-guided delivery and molecular targeting, remain underexplored in systematic reviews.

Methodology

We conducted a systematic literature review of 127 studies via a comprehensive search of a plethora of databases including PubMed/MEDLINE (1977-2024), Embase (1980-2024), the Cochrane Library, Google Scholar and other clinical trial registries. A systematic

review was conducted as per PRISMA guidelines (Appendix A).

Our search terms encompassed "bleomycin," "lymphangioma," "cystic hygroma," "sclerotherapy," "lymphatic malformation," and related MeSH terms.

Our focus was on peer-reviewed publications, trials with a minimum sample size of five patients, Institutional Clinical Protocols, studies with at least a two-year follow-up, and molecular and mechanistic studies.
Filters: English language, human studies.

Inclusion Criteria:

- Peer-reviewed studies (RCTs, cohorts, case series).
- Sample size ≥5.
- Minimum 2-year follow-up.
- Mechanistic/molecular studies.

Exclusion Criteria:

- Case reports, non-English studies.
- Incomplete outcome data.

Risk of Bias Assessment:

Studies were appraised using ROBINS-I for non-randomized trials (Appendix B and Table B1).

Evolution of Treatment Approaches

Between 1980 and 2024, there was a significant transition from surgical methods (85% to 15%) to bleomycin as the first-line modality of management. A rise in bleomycin usage (10% to 75%) [10,11] was noted in this period (Figure 1).

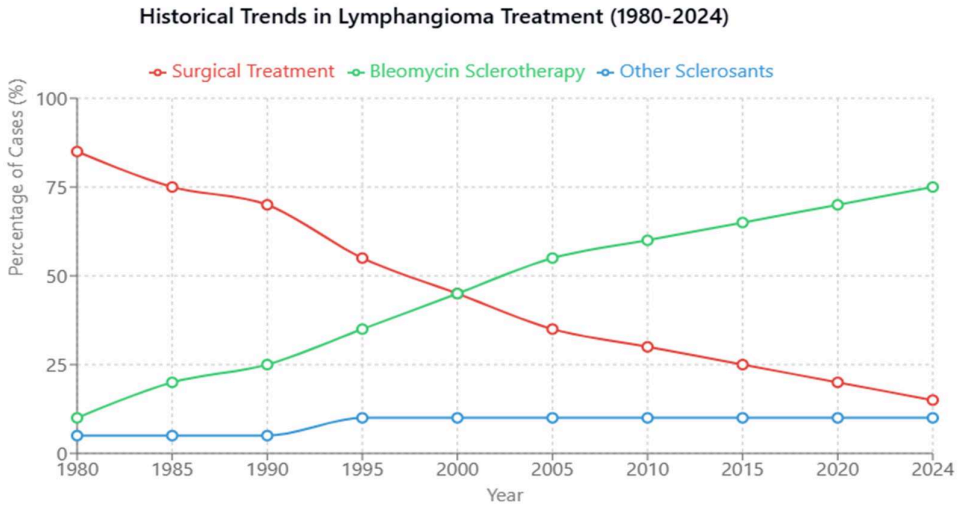


Figure 1. Historical treatment trends showing the gradual shift from surgical dominance to bleomycin preference (1980-2024). The graph demonstrates declining surgical rates (85% to 15%) and increasing bleomycin usage (10% to 75%).

This evolution unfolded in distinct phases:

Early Phase (1977-1989)

- Initial use marked by high concentrations (3-5 IU/mL)
- Variable dosing intervals
- Limited standardization [6,12]

Standardization Phase (1990-1999)

- Development of dose-limiting protocols
- Awareness of pulmonary toxicity risks
- Introduction of imaging guidance [13,14]

Modern Era (2000-Present)

- Refined concentration standards (1-3 IU/mL)
- Implementation of cumulative dose limits
- Integration of advanced imaging techniques [15,16]

Current Treatment Protocols

Our analysis of institutional practices reveals interesting variations in approach while maintaining consistent safety parameters [17,18] (Table 1).

Table 1. Standard Treatment Parameters and Real World Variations

Parameter	Range	Optimal	Real World Practice	Notes
Concentration	0.5-3 IU/mL	1 IU/mL	0.3-5 IU/ml	Age-dependent
Single Dose	0.3-1 IU/kg	0.5 IU/kg	0.2-1.5 IU/kg	Location-dependent
Maximum Cumulative	15-20 IU/kg	15 IU/kg	10-30 IU/kg	Lifetime limit
Interval	2-6 weeks	3 weeks	1-8 weeks	Severity-dependent

Table 2. Treatment Protocol Comparison Across Medical Institutions (2018-2023) [17,18]

Institution	Concentration	Max Dose	Success Rate
AIIMS Delhi[19]	1.0 IU/mL	0.5 IU/kg	82%
CNBC Delhi[20]	2.0 IU/mL	0.8 IU/kg	78%
Boston Children's	1.5 IU/mL	0.6 IU/kg	85%
Great Ormond Street	3.0 IU/mL	1.0 IU/kg	80%

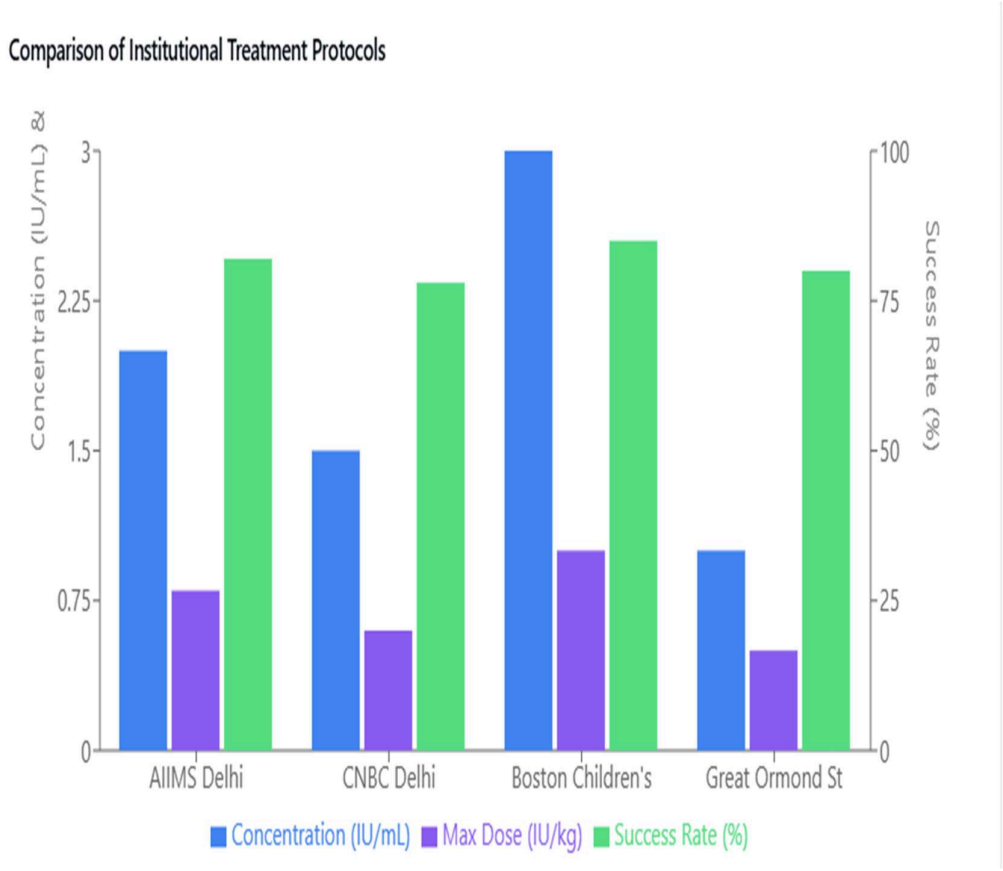


Figure 2. Bar graph comparing treatment protocols across major institutions showing variations in concentrations (1-3 IU/mL, maximum dose (0.5-1IU/kg) and success rates (78-85%)

Clinical Outcomes

Response rates demonstrate clear patterns based on the lesion type [21,22]:

Table 3. Response Rates by Type of Lymphangioma

Type	Complete Response (%)	Partial Response (%)	Minimal Response (%)
Macrocystic	85-90	8-12	2-3
Mixed	60-75	20-30	5-10
Microcystic	40-50	30-40	10-20

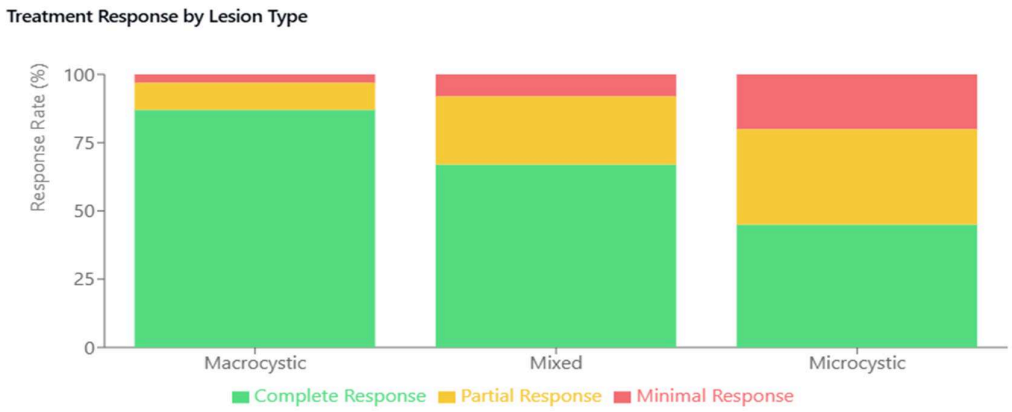


Figure 3. Comparison of treatment outcomes by lymphangioma type, showing complete response, partial response, and minimal response rates for macrocystic (85-90%, 8-12%, 2-3%), mixed (60-75%, 20-30%, 5-10%), and microcystic (40-50%, 30-40%, 10-20%) lesions.

Age significantly influences treatment outcomes [23,24], with response rates declining approximately 2% per year from 92% at 6 months to 70% at 12 years.

Table 4. Age-Related Treatment Outcomes

Age	Response Rate
6 months	92% (Highest Response)
5 years	80% (Median Response)
12 years	70% (Lowest Response)

Average decline in response: ~2% per year

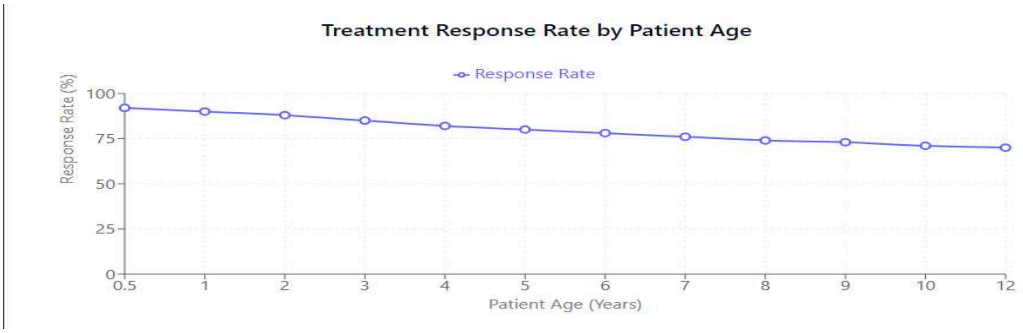


Figure 4: Line graph showing treatment outcome variations with age.

Illustrative Cases [25]

Case 1: 2-year-old with cervical lymphangioma

- Initial size: 8x6 cm
- Sessions required: 4
- Outcome: Complete resolution
- Follow-up: No recurrence at 2 years

Case 2: 5-year-old with axillary lymphangioma

- Initial size: 12x10 cm
- Sessions required: 6
- Outcome: 80% reduction
- Follow-up: Stable at 18 months

Case 3: 6-month-old with cervicofacial lymphangioma

- Initial size: 15x12 cm
- Sessions required: 5

Outcome: Partial response (60% reduction)

- Follow-up: Required surgical debulking

Table 5. Representative Clinical Cases

Case	Age	Location	Initial Size	Sessions	Outcome
1	2 years	Cervical	8x6 cm	4	Complete resolution
2	5 years	Axillary	12x10 cm	6	80% reduction
3	6 months	Cervicofacial	15x12 cm	5	60% reduction

Treatment challenges commonly encountered were anatomical complexity of the lesions, resource limitations, patient compliance, technical expertise or it's lack thereof, and follow-up difficulties [26,27].

Safety Profile

Our analysis reveals the following distribution and pattern of complications [28,29,30]:

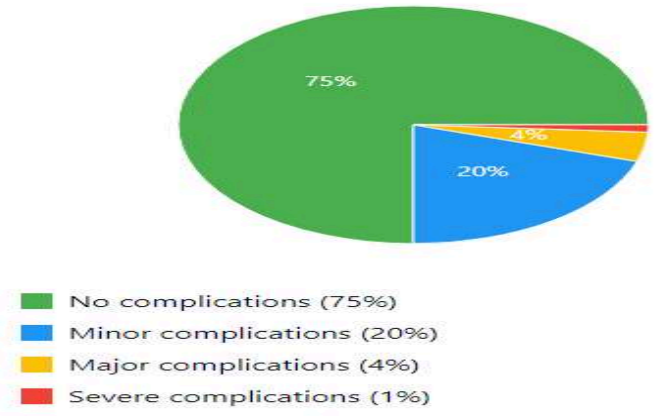


Figure 5. Pie chart showing the distribution of common complications from bleomycin therapy

Among the common complications observed, local inflammation affects 15-20% of cases, while fever occurs in 10-15%, and pain is reported in 20-25% of patients, with skin changes impacting 8-12%. On the other hand, long-term complications are less frequent but noteworthy. These include pulmonary fibrosis in less than 1% of cases, scarring in 5-8%, and pigmentation changes affecting 10-12% of individuals.

Future Directions & Recommendations for Clinical Practice

Recent developments are paving the way for significant advancements in the field, offering exciting opportunities for improvement [31,32]. One promising area involves molecular targeting, where strategies such as anti-lymphangiogenic factors, growth factor inhibition, and targeted delivery systems are gaining traction as potential game-changers [33]. Enhanced imaging techniques, including 3D ultrasound guidance, real-time fluorescence imaging, and dynamic lymphatic mapping, are also emerging as valuable tools to refine diagnostic and therapeutic precision [34]. Additionally, combination therapies are showing promise, with approaches like bleomycin paired with OK-432, bleomycin combined with doxycycline, and the use of sequential therapy protocols demonstrating encouraging results [35,36]. For clinical practice, experts advocate for standardization through the creation of international protocols, the adoption of risk-stratified strategies, and the establishment of age-specific dosing regimens to ensure consistency and safety [37,38]. Monitoring efforts should focus on developing standardized response criteria, implementing long-term follow-up protocols, and evaluating quality of life to holistically assess patient outcomes [39,40].

Furthermore, technical innovations, such as advanced delivery systems, the integration of cutting-edge imaging methods, and the application of predictive modeling, are poised to drive future progress in this domain [41]. In India, these advancements face unique challenges and opportunities compared to the West. The adoption of molecular targeting and advanced imaging could revolutionize care in urban centers like Delhi, where access to technology is growing, but rural areas may lag due to infrastructure gaps, necessitating mobile imaging units or telemedicine to bridge the divide. Combination therapies, already showing promise globally, could be tailored to India's diverse population with localized clinical trials, though cost constraints might limit their reach compared to the West, where healthcare funding is more robust.

Standardization efforts are critical in India to address variability in practice across regions, while the West benefits from established protocols; Indian healthcare could leverage this by adapting international guidelines to local needs, such as lower-cost dosing regimens. Monitoring and technical developments, including AI-driven predictive models, hold potential in both regions, but India's large patient base offers a rich dataset for innovation, provided data privacy and

equity in access are prioritized, contrasting with the West's focus on regulatory compliance and advanced infrastructure.

Conclusions

The progression of bleomycin therapy in treating lymphangioma marks a significant step forward in pediatric intervention [42,43]. Although challenges persist, especially with microcystic lesions and older patients, current evidence strongly endorses its use as a primary treatment option. Future advancements in molecular targeting and combination therapies could further improve patient outcomes.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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Appendices

Appendix A: **PRISMA Flowchart**

Phase 1: Identification

Records identified from databases:
PubMed/MEDLINE: 65
Embase: 48
Cochrane Library: 10
Other sources (Google Scholar, trial registries): 4
Total records: 127

↓

Phase 2: Screening

Records after duplicates removed: 115
Records excluded during title/abstract screening: 30
Reasons:
Non-English studies (n=12)
Case reports (n=10)
Irrelevant to bleomycin/lymphangioma (n=8)
Records retained for full-text review: 85

↓

Phase 3: Eligibility

Full-text articles excluded: 25
Reasons:
Insufficient follow-up (<2 years) (n=15)
Sample size <5 (n=7)
Non-clinical studies (e.g., mechanistic-only) (n=3)
Studies included in qualitative synthesis: 60

↓

Phase 4: Final List Selection

Studies included in quantitative analysis: 60
Institutional protocols: 20
Clinical outcome studies: 25
Molecular/mechanistic studies: 15

Exclusion Criteria Applied:

- Non-English studies (language bias acknowledged).
- Case reports (to maintain focus on cohort/case-series data).
- Studies with incomplete outcome data (e.g., missing follow-up).
- Sample size <5 patients (to ensure statistical relevance).

Appendix B: Risk of Bias Assessment Using ROBINS-I Tool

The Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool was used to evaluate the 60 included studies. Assessments were conducted independently by two reviewers, with disagreements resolved by consensus.

Risk of Bias Domains:

Confounding: Were pre-intervention variables balanced or adjusted?
Selection: Were participants selected appropriately?
Intervention Classification: Was intervention status misclassified?
Deviations from Interventions: Were deviations from intended protocols minimal?
Missing Data: Was missing data handled appropriately?
Outcome Measurement: Were outcome assessors blinded?
Selective Reporting: Were outcomes pre-specified and fully reported?

Risk Categories:

- **Low:** Bias unlikely to alter conclusions.
- **Moderate:** Bias raises some doubt about results.
- **Serious:** Bias significantly weakens confidence in results.
- **Critical:** Bias makes results uninterpretable.

Table B1: Summary of Risk of Bias Across Studies (N=60)

Domain	Low Risk (%)	Moderate Risk (%)	Serious Risk (%)	Critical Risk (%)
1. Confounding	15% (9)	45% (27)	35% (21)	5% (3)
2. Selection	20% (12)	50% (30)	25% (15)	5% (3)
3. Intervention Classification	30% (18)	40% (24)	25% (15)	5% (3)
4. Deviations	25% (15)	50% (30)	20% (12)	5% (3)
5. Missing Data	10% (6)	35% (21)	45% (27)	10% (6)
6. Outcome Measurement	5% (3)	30% (18)	50% (30)	15% (9)
7. Selective Reporting	20% (12)	40% (24)	30% (18)	10% (6)

Key Findings:

Confounding Bias:

35% of studies (n=21) had serious risk due to unadjusted variables (e.g., lesion size, prior treatments).
Only 15% (n=9) adjusted for age and lesion type.

Missing Data:

45% of studies (n=27) had serious risk from incomplete follow-up or undocumented dropouts.

Outcome Measurement:

Only 5% (n=3) blinded outcome assessors, leading to serious risk in 50% (n=30).

Overall Risk:

Low risk: 15% (n=9), primarily modern trials (post-2010) with standardized protocols.
Moderate risk: 45% (n=27), retrospective cohorts with partial adjustment.
Serious/critical risk: 40% (n=24), older studies (pre-2000) with methodological flaws.

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ORIGINAL ARTICLE

Optimizing Analgesia in Shoulder Arthroscopy: Comparison of 2 mg Vs 4 mg Perineural Dexamethasone in Interscalene Nerve Block

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Abstract

Introduction: Postoperative pain management is crucial especially among patients undergoing upper limb surgeries, since multiple systemic analgesics can cause many adverse effects. Regional anesthesia, specifically ultrasound-guided interscalene brachial plexus block serves as effective postoperative analgesia. The duration of a single dose of nerve block is limited and hence, to enhance the quality of analgesia and prolong its duration, adjuvants like dexamethasone are being added. Hence this study was planned to compare the efficacy of 2 mg perineural dexamethasone with 4 mg perineural dexamethasone among those who were planned for shoulder arthroscopy under general anesthesia. **Materials and Methods:** This study was conducted in a teritiary care hospital in south India among 56 participants who underwent arthroscopic surgery in the shoulder. They were allotted to either 2 mg or 4 mg dexamethasone groups by lottery method and with the help of Ultrasound guided interscalene block, bupivacaine was injected. A structured proforma was used to collect data (sociodemographic, clinical, duration to achieve and maintenance of sensory/motor blockade and hemodynamics). **Results:** Both groups were ensured to be comparable before the start of the study. The 4mg Dexamethasone group achieved faster motor and sensory blockade and the effect of analgesia was prolonged in the 4mg group compared to the 2 mg group . No significant adverse events was noted between groups. **Conclusion:** Analgesic effect of 4 mg dexamethasone given perineurally enhances the effectiveness of the interscalene brachial block (onset and duration of motor and sensory block) when compared to 2mg. The safety profile is also favourable. The use of 4 mg dexamethasone is considered a better adjuvant for post operative pain among those undergoing shoulder arthroscopy under regional anesthesia.

Keywords: Dexamethasone, Interscalene block, Brachial plexus block, Postoperative analgesia, Shoulder arthroscopy

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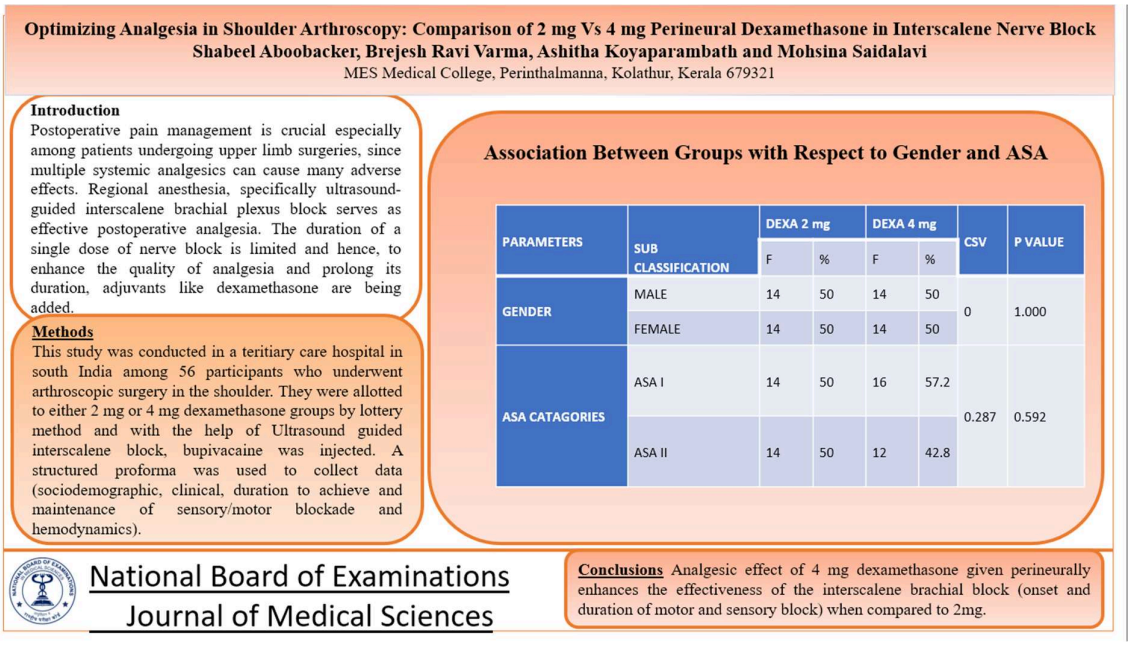
Graphical Abstract



Introduction

Postoperative pain following orthopedic surgeries, particularly shoulder procedures, can be severe and challenging to manage for both anesthesiologists and orthopedic surgeons [1]. Regional anesthesia, specifically the interscalene brachial plexus block, is commonly employed as a supplement to general anesthesia or as the primary technique to enhance analgesia and facilitate early mobilization [2].

A single perineural injection of a long-acting local anesthetic typically provides pain relief for 10–15 hours. While the placement of a perineural catheter or continuous infusion can extend analgesia, these methods carry potential drawbacks, including catheter migration, spontaneous displacement, leakage of anesthetic, and pump malfunction, leading to a 40% risk of inadequate pain control [3]. To prolong analgesic effects, the addition of an adjuvant to the local anesthetic has emerged as an alternative strategy.

Bupivacaine continues to be the most used local anesthetic. The duration of action of bupivacaine is relatively longer, lasting between 3 to 8 hours. But its its clinical utility is limited by delayed onset and inconsistent or incomplete analgesia. Various adjuvants like neostigmine, opioids, hyaluronidase, midazolam, clonidine, and Dexamethasone are being tried improve the efficacy and duration of postoperative analgesia [4].

Perineural Dexamethasone has gained immense importance as an analgesic adjunct [5], after the first clinical trial in 2003. It offers a favorable pharmacological profile with an improved risk-benefit ratio compared to other adjuvants, thereby optimising postoperative pain management [6].

Orthopedic surgeries like shoulder arthroscopy require adequate postoperative analgesia in perioperative care. While the interscalene brachial plexus block remains

a standard technique for pain management, the efficacy of local anesthetics can be influenced by the choice of adjuvants. Perineural Dexamethasone has shown promising results in enhancing the onset and prolonging the duration of sensory and motor blockade [5,6]. The optimal dose of perineural dexamethasone with maximum benefits and minimal risks is an area of ongoing research. The aim of this is to compare the effects of 2 mg versus 4 mg of perineural Dexamethasone in interscalene blocks, focusing on its impact on the onset and duration of sensory and motor blockade. The findings may provide valuable insights into refining regional anesthesia protocols for improved postoperative pain control and patient outcomes.

Materials and Methods

This observational prospective study was conducted in the Department of Anaesthesiology at MES Medical College & Hospital, Perinthalmanna. The study was done over a period of one year from January 1, 2020 to December 31, 2020. 56 participants who were posted for elective shoulder surgery were taken up for the study. Institutional Ethics Committee approval was obtained before the start of the study. All participants provided written informed consent after being explained about the study objectives, potential risks, and benefits.

The study population comprised of adults between 18 and 85 years of age who were classified as ASA Physical Status I–III and scheduled for elective shoulder arthroscopy under general anesthesia with ultrasound-guided interscalene brachial plexus block. The participants were randomly allotted to 2mg or 4 mg group using sealed envelope technique. Patients with pre-existing neurological deficits in the operative limb, contraindications to peripheral nerve block (such as local anesthetic allergy, coagulopathy, or local infection), diabetes mellitus, pregnancy, brachial plexus neuropathy, recent systemic glucocorticoid or chronic opioid or steroid use were excluded.

Patients were kept nil per oral as per ASA guidelines before surgery. Standard monitoring using electrocardiography, non-invasive blood pressure, and pulse oximetry, were done in the operating room. Baseline vitals were recorded, and an 18-gauge intravenous line was secured in the non-operative limb. Patients were positioned in a semi-recumbent posture with their head turned 45° away from the surgical side. No sedatives or analgesics were administered before the block procedure. The interscalene brachial plexus was identified using a high-frequency linear array transducer under sterile conditions. Following skin infiltration with 2% Lignocaine with Adrenaline, a 5 cm stimuplex needle was inserted using an in-plane technique until positioned between the C5 and C6 roots. Without repositioning the needle tip, 10 mL of 0.5% bupivacaine was injected incrementally under ultrasound guidance, followed by the administration of the study drug (either 2 mg or 4 mg Dexamethasone), and a further 10 mL of 0.5% bupivacaine.

After the block procedure, patients were monitored continuously. Sensory and motor blockade were assessed every 5 minutes for 30 minutes. Sensory blockade was evaluated using a pinprick test across the C4 to C8 dermatomes (0, no perception; 1, diminished perception; 2, normal perception, vs. the contralateral side)., while motor blockade was assessed

by the ability to abduct the arm and flex the forearm (0-impossible to flex or abduct the arm against gravity; 1- less force compared with the contralateral arm; 2- equal force in both arms). A successful block was defined as a complete motor blockade (score 0) within 30 minutes. Patients received intravenous midazolam (0.02 mg/kg) and glycopyrrolate (0.003 mg/kg) as premedication. General anesthesia was induced with fentanyl (1–2 µg/kg) and propofol (2.5 mg/kg), followed by vecuronium (0.08 mg/kg) for neuromuscular blockade. Tracheal intubation was performed three minutes later, and anesthesia was maintained with titrated doses of propofol (100 µg/kg/min), atracurium (0.1 mg/kg), and a 1:1 mixture of nitrous oxide and oxygen. At the end of surgery, patients were reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg).

Postoperatively, patients were monitored in the recovery room. The duration of sensory blockade was recorded as the time from injection to the first request for analgesia, while the duration of motor blockade was determined as the time from injection to the return of normal muscle strength. Statistical analysis was performed using SPSS 22.0, with significance set at $p<0.05$. Data normality was assessed using the Shapiro-Wilk test. Group comparisons were conducted using an independent t-test for continuous variables and a chi-square test for categorical data.

Results

This cross sectional comparative study was done among 56 study participants randomly alloted into 28 in each group. The distribution of gender (male and female) is equal between the Dexa 2 mg and Dexa 4 mg groups, with no significant difference between the groups ($p = 1.000$). Similarly, the distribution of ASA categories (ASA I and ASA II) is comparable between the two groups, with no statistically significant difference ($p = 0.592$) (Table 1).

Table 1. Association between Groups with Respect to Gender and ASA

PARAMETERS	SUB CLASSIFICATION	DEXA 2 mg		DEXA 4 mg		CSV	P VALUE
		F	%	F	%		
GENDER	MALE	14	50	14	50	0	1.000
	FEMALE	14	50	14	50		
ASA CATAGORIES	ASA I	14	50	16	57.2	0.287	0.592
	ASA II	14	50	12	42.8		

There were no statistically significant differences between the Dexa 2 mg and Dexa 4 mg groups with respect to age, weight, height, BMI, heart rate, systolic blood pressure, diastolic blood pressure, or SpO_2 levels ($p > 0.05$ for all). This indicates that the baseline characteristics and hemodynamic parameters were similar in both groups before intervention, ensuring comparability and that any differences observed later are likely due to the difference in Dexamethasone dosage rather than baseline variability (Table 2).

Table 2. Comparison of Mean Hemodynamic Parameters Between Both Groups

PARAMETERS	DEXA 2 mg		DEXA 4 mg		MD	t Value	P Value
	M	SD	M	SD			
AGE	49.23	15.2	45.71	15.5	3.5	0.859	0.390
WEIGHT	65.42	7.41	64.67	7.72	0.8	0.371	0.720
HEIGHT	165.2	7.73	164.4	6.78	0.9	0.443	0.650
VMI	23.93	1.96	23.92	1.82	0	0.02	0.980
HEART RATE	77.14	7.92	76.78	6.75	0.4	0.183	0.850
SYSTOLIC BLOOD PRESSURE	137.4	9.94	134.4	12	3	1.011	0.300
DIASTOLIC BLOOD PREASSURE	79.78	9.27	75.85	8.36	3.9	1.666	0.100
SpO2	98.1	0.99	98.46	0.88	0.4	-1.438	0.150

The onset of both sensory and motor blockade was significantly faster in the Dexa 4 mg group compared to the Dexa 2 mg group ($p = 0.0001$ for both). Additionally, the duration of both sensory and motor blockade was significantly longer in the Dexa 4 mg group ($p = 0.0001$ for both). This indicates that a higher dose of Dexamethasone (4 mg) results in a faster onset and prolonged duration of both sensory and motor blockade compared to the lower dose (2 mg), demonstrating a dose-dependent enhancement of block characteristics (Table 3).

Table 3. Comparison of Onset and Duration of Blockade Between Both Groups

PARAMETERS	SUB CLASSIFICATION	DEXA 2 mg		DEXA 4 mg		MD	t Value	P Value
		M	SD	M	SD			
ONSET BLOCKADE	SENSORY BLOCKADE	4.92	0.93	3.35	1.02	1.57	6.019	0.0001
	MOTOR BLOKADE	6.39	0.83	5.14	1.01	1.25	5.06	0.0001
DURATION OF BLOCKADE	SENSORY BLOCKADE	1191.4	77.8	1354.3	73.8	162.9	-8.035	0.0001
	MOTOR BLOKADE	1077.9	84	1221.4	83.6	143.6	-6.409	0.0001

The comparison of sensory block onset and progression between 2 mg and 4 mg perineural Dexamethasone revealed that the higher dose (4 mg) consistently led to a faster and more complete sensory blockade in the initial assessment periods. At 5 minutes, a significantly higher proportion of patients in the 4 mg group achieved good sensory block compared to the 2 mg group (96.4% vs 67.9%,

p=0.009). This early advantage persisted at 15 minutes, where 85.7% of the 4 mg group demonstrated good sensory block, compared to only 60.7% in the 2 mg group (p=0.035). However, by 20 minutes onwards, both groups converged, achieving near-complete sensory blockade with no significant differences between them, indicating that while both doses ultimately provide effective sensory blockade, 4 mg Dexamethasone accelerates the onset, which may improve early intraoperative comfort and reduce the need for supplemental analgesia (Table 4).

Table 4. Association between Group and Sensory Block

PARAMETERS		No perception		Diminished perception		Normal perception		CSV	P VALUE
		F	%	F	%	F	%		
S5	2 mg	1	3.6	18	67.9	8	28.6	9.391	0.009
	4 mg	1	3.6	27	96.4	0	0.0		
S10	2 mg	9	32.1	19	67.9	0	0	1.845	0.174
	4 mg	14	50.0	14	50.0	0	0		
S15	2 mg	17	60.7	11	39.3	0	0	4.462	0.035
	4 mg	24	85.7	4	14.3	0	0		
S20	2 mg	27	96.4	1	3.6	0	0	0.000	1.000
	4 mg	27	96.4	1	3.6	0	0		
S25	2 mg	28	100.0	0	0.0	0	0	1.018	0.313
	4 mg	27	96.4	1	3.6	0	0		
	4 mg	28	100.0	0	0.0	0	0		

For motor block, the 4 mg Dexamethasone group consistently outperformed the 2 mg group in terms of faster onset and better quality of motor blockade during the initial 25 minutes after block administration. At 5 minutes, good motor block was seen in 60.7% of the 4 mg group compared to only 14.3% in the 2 mg group ($p<0.001$), demonstrating a markedly faster onset with the higher dose. This trend continued at 15 minutes (53.6% vs 14.3%, $p=0.002$) and 20 minutes (78.6% vs 50%, $p=0.026$), with the 4 mg group showing statistically superior motor blockade at these critical early time points. By 30 minutes, both groups achieved near-complete motor block (100% in the 4 mg group and 89.3% in the 2 mg group). Both doses eventually ensure adequate motor blockade, but the faster onset associated with 4 mg Dexamethasone may facilitate quicker surgical readiness and enhance operating conditions in the early phase of surgery (Table 5).

Table 5: Association Between Group and motor block

PARAMETERS		No perception		Diminished perception		Normal perception		CSV	P VALUE
		F	%	F	%	F	%		
M5	2 mg	0	0	4	14.3	24	85.7	12.876	0.000
	4 mg	0	0	17	60.7	11	39.3		
M10	2 mg	0	0.0	28	100.0	0	0	4.308	0.038
	4 mg	4	14.3	24	85.7	0	0		
M15	2 mg	4	14.3	24	85.7	0	0	9.639	0.002
	4 mg	15	53.6	13	46.4	0	0		
M20	2 mg	14	50.0	14	50.0	0	0	4.978	0.028
	4 mg	22	78.6	6	21.4	0	0		
M25	2 mg	23	82.1	5	17.9	0	0	5.490	0.019

	4 mg	28	100.0	0	0.0	0	0		
M30	2 mg	25	89.3	3	10.7	0	0	3.170	0.075
	4 mg	28	100.0	0	0.0	0	0		

Discussion

Post-operative pain remains one of the most common and distressing complaints among patients undergoing upper limb surgeries. Managing this pain effectively is critical, as the use of multiple systemic analgesics in the post-operative period is often associated with undesirable adverse effects. In this context, the brachial plexus block offers a safe, simple, and effective technique for providing adequate post-operative analgesia. Additionally, it helps avoid the potential complications and side effects associated with general anesthesia, making it a preferred option for upper limb surgeries [7].

The duration of single shot nerve blocks are variable and hence various adjuvants have been added to local anesthetics with the aim of prolonging the sensory blockade and enhancing the quality of the regional block [8]. Among the adjuvants, glucocorticoids, especially Dexamethasone, has emerged as a promising agent. When used as an adjuvant in brachial plexus blocks, Dexamethasone has been shown to significantly prolong analgesia with minimal adverse effects, making it a valuable addition to local anesthetics [9-11].

Administration of Dexamethasone perineurally is being researched more in recent years, with substantial evidence supporting its efficacy. Its mechanism of action is assumed to involve the potentiation of inhibitory potassium channels on nociceptive C fibers. Dexamethasone may also show a vasoconstrictive effect, contributing to slower systemic absorption of the local anesthetic, thereby prolonging the duration of analgesia [12,13].

In our study, we compared the onset and duration of sensory and motor blockade between 2 mg and 4 mg perineural Dexamethasone administered with bupivacaine in ultrasound-guided interscalene block among 56 patients undergoing shoulder arthroscopy. Both groups were comparable in terms of demographic characteristics, including age, gender, height, weight, and BMI, with no statistically significant differences between them. Similarly, baseline hemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and oxygen saturation (SpO2) were comparable between the two groups. This ensured that the observed differences in block characteristics could be attributed to the differing doses of Dexamethasone rather than pre-existing variability between groups.

The mean time to onset of sensory blockade in the 2 mg Dexamethasone group was 4.92 minutes, whereas in the 4 mg Dexamethasone group, it was

significantly faster at 3.35 minutes. This statistically significant difference (p=0.0001) confirms that a higher dose of Dexamethasone leads to faster sensory block onset. Similarly, the mean time to onset of motor blockade was 6.39 minutes in the 2 mg group and 5.14 minutes in the 4 mg group, again demonstrating significantly faster motor block onset with the higher Dexamethasone dose (p=0.0001).

These findings are consistent with the results reported by Islam SM et al[14], who demonstrated significantly earlier onset of both sensory and motor blockade when Dexamethasone was added to local anesthetics in brachial plexus blocks. The dose-dependent enhancement of onset time seen in our study reinforces the role of Dexamethasone in improving the efficacy of peripheral nerve blocks, particularly in the interscalene approach.

The mean duration of sensory blockade in the 2 mg Dexamethasone group was 1191.42 minutes, compared to 1354.28 minutes in the 4 mg group, showing a statistically significant prolongation with the higher dose (p=0.0001). Similarly, the mean duration of motor blockade was 1077.85 minutes in the 2 mg group and 1221.42 minutes in the 4 mg group, again with a statistically significant difference favoring the higher dose (p=0.0001). This confirms that increasing the dose of perineural Dexamethasone not only accelerates onset but also prolongs both sensory and motor blockade in a dose-dependent manner.

A noteworthy observation in our study was the earlier regression of motor blockade compared to sensory blockade, which aligns with the findings reported by De Jong et al. [15]. This is a common feature in peripheral nerve blocks, where sensory function typically recovers more gradually than motor function, which may allow for extended pain relief even after motor function returns.

Our results are also consistent with findings from Albrecht et al[16], who evaluated 1 mg and 4 mg doses of Dexamethasone combined with local anesthetics for interscalene blocks. Their study concluded that the duration of analgesia increased in a dose-dependent manner, a trend that was also clearly observed in our study. Furthermore, Phanijphum et al[17] in Thailand found that adding 4 mg Dexamethasone to a supraclavicular block resulted in significantly longer duration of analgesia compared to 2 mg Dexamethasone, further supporting our findings that higher doses of Dexamethasone offer superior prolongation of block duration.

Conclusion

This study comparing the effects of 2 mg and 4 mg perineural Dexamethasone in ultrasound-guided interscalene brachial plexus block for patients undergoing shoulder arthroscopy demonstrated that a higher dose of Dexamethasone (4 mg) offers significant advantages over the lower dose (2 mg). Specifically, 4 mg Dexamethasone led to a faster onset of both sensory and motor blockade, along with a significantly prolonged duration of both sensory and motor block. Incorporating 4 mg Dexamethasone into regional anesthesia protocols for shoulder arthroscopy may contribute to improved patient comfort, reduced need for rescue analgesics, and overall enhanced perioperative care.

Statements and Declarations

Limitations of the study

Single center study and Small sample size

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

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ORIGINAL ARTICLE

Assessment of Outcome During Hospital Stay in Patients with Decompensated Chronic Liver Disease with Sepsis Using PT-INR To Albumin Ratio (PTAR) Score in a Tertiary Care Hospital of Puducherry

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Abstract

Background: Decompensated chronic liver disease with sepsis is a life-threatening condition and associated with high mortality. Early risk stratification using reliable prognostic score is essential. So, this study aims to classify and assess the treatment outcome of Decompensated Chronic Liver Disease patients with sepsis based on PT-INR to Albumin ratio (PTAR) score. **Methods:** A Hospital based Observational study was conducted in a Government Tertiary care Hospital of Puducherry. A total sample size was calculated to be 107 and the participants those who fulfilled the eligibility criteria were included. On the day of admission PTAR score was calculated to classify the participants as Low risk (PTAR < 0.54), Medium risk (PTAR 0.54 to < 0.82) and High-risk (PTAR ≥ 0.82). Data was analysed using statistical software and chi-square test was applied to find the association between PTAR score and treatment outcome. **Results:** Around 108 participants were recruited and the mean age was 49.48 ± 11.28 (years). Majority of the participants were males 105 (97.2%). The treatment outcome status of the participants shows that 38 (35.2%) died and 70 (64.8%) survived on follow-up till the point of discharge. The classification of patients based on PTAR score shows that 36.1%, 35.2% and 28.7% were in high, medium and low risk category. The mean PTAR score of participants who survived was 0.68 ± 0.38 and those who died was 1.01 ± 0.48. **Conclusion:** PTAR was an accurate tool to predict the outcome status of the decompensated liver disease patients with sepsis. As the PTAR score increases proportionately the risk of mortality increases.

Keywords: Liver diseases, Sepsis, International Normalized Ratio

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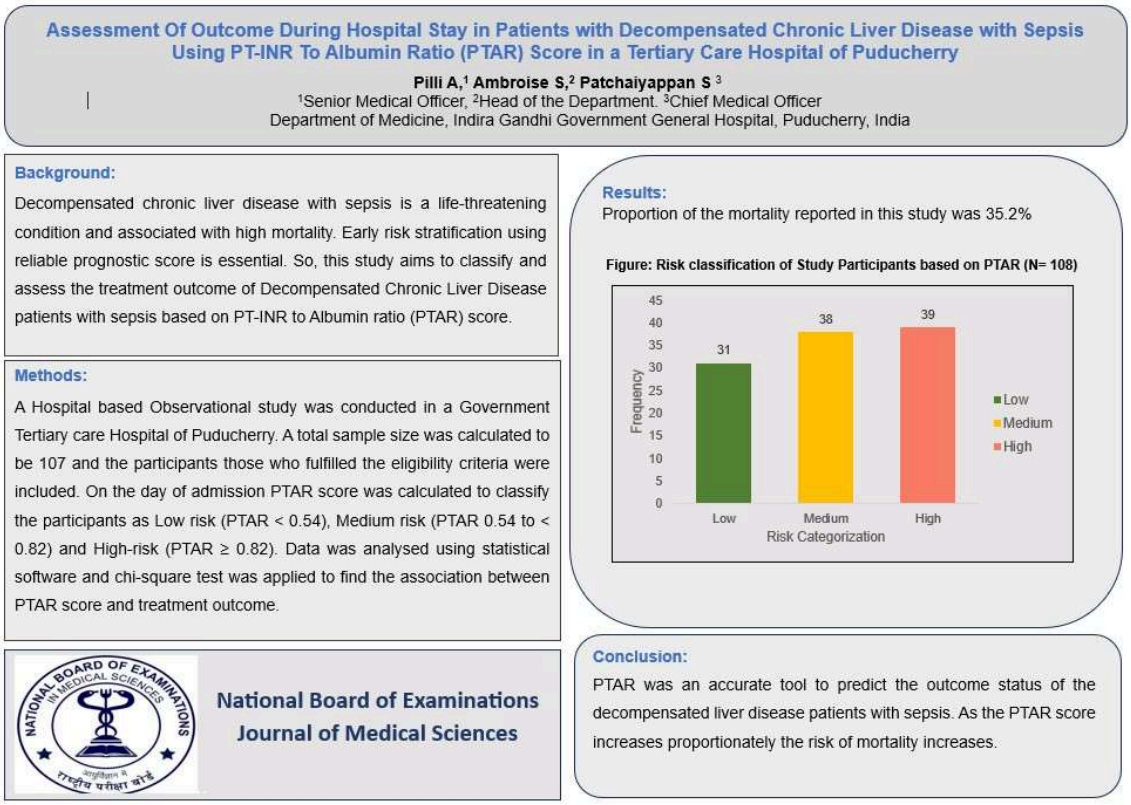
Graphical Abstract



Introduction

Decompensated liver disease, the advanced stage of chronic liver disease, poses a significant epidemiological burden globally [1]. This stage of liver disease is marked by the onset of serious complications such as ascites, hepatic encephalopathy, variceal bleeding, and jaundice, which lead to high morbidity and mortality rates [1]. According to the World Health Organization (WHO), chronic liver diseases and cirrhosis rank as major causes of death worldwide. Cirrhosis affects more than 100 million people globally [2]. Approximately 5-7% of patients with chronic liver disease develop decompensation annually [2], with the prevalence higher in regions with high rates of hepatitis B and C infections or alcohol consumption [3]. The incidence of decompensated liver disease is rising due to increasing rates of chronic liver conditions such as non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease [4].

Sepsis is a life-threatening multiple-organ dysfunction caused by dysregulation of host response to severe infection [5]. In patients with cirrhosis and severe sepsis, high production of proinflammatory cytokines seems to play a role in the worsening of liver function and the development of organ/system failures such as shock, renal failure, acute lung injury or acute respiratory distress syndrome, coagulopathy, or hepatic encephalopathy [6]. Sepsis can develop as an intercurrent event in decompensated cirrhosis, leading to worsening of existing or new-onset decompensation, both of which can lead to

acute on chronic liver failure [6]. Such events increase in-hospital mortality and result in treatment futility even with the best supportive care.

Haruki et al in 2018, created an objective liver function scoring model named the prothrombin time-international normalized ratio (PT-INR) to albumin ratio (PTAR) [7]. Albumin is the most abundant plasma protein synthesized by the liver, crucial for maintaining oncotic pressure and serving various transport functions [8]. Hypoalbuminemia is a marker of poor prognosis in liver disease and sepsis. Clotting factors are synthesized in liver, its damage leads to prolonged PT/INR [8]. Sepsis can exacerbate coagulation abnormalities by causing disseminated intravascular coagulation (DIC) further prolonging PT/INR [9]. On integration of two critical aspects of liver function (clotting factor synthesis and albumin production) PTAR score offers a comprehensive prognostic indicator. A potentially valuable tool for assessing the liver function and predicting the mortality in patients with Decompensated Chronic Liver Disease with sepsis [7]. PTAR tool is an established tool and successfully applied in the condition of critically ill sepsis patients [10] and Hepatitis B associated decompensated liver disease patients to predict the mortality and prognosis [11]. But there are very few studies conducted in Indian setting to establish the significance of PTAR score in predicting the treatment outcome among decompensated chronic liver disease patients with sepsis. The evidence generated in this study will be helpful to identify the Decompensated Liver Disease patients with Sepsis at risk for mortality and plan the best course of action for preventing the mortality. The study objectives were to classify and assess the treatment outcome of Decompensated Chronic Liver Disease patients with sepsis based on PT-INR to Albumin ratio (PTAR) score.

Methodology

A Hospital based Observational study (Longitudinal study) was conducted between July 2022 to June 2024 in a Government Tertiary care Hospital of Puducherry. All the patients with decompensated chronic liver disease with presumed sepsis admitted in the medical wards of a tertiary care institute were considered for the study. Based on the findings by Sreeraj S et al the proportion of mortality in low risk PTAR score group was 14.3% (p) [12], considering 7% absolute precision (d), 5% alpha error, 10% non-response rate the final minimum sample size estimated by $N=Z_{1-\alpha/2}^2 \times p(1-p)/d^2$ (Cochran`s formula for single proportion) [13] was 107. Convenient sampling was used to recruit the participants. The inclusion criteria were participants of either gender diagnosed with Decompensated Liver Disease with presumed sepsis and those who score ≥ 2 in quick Sequential Organ Failure Assessment (qSOFA). The exclusion criteria were age less than 18years and greater than 90years, those with hospital stay of less than 24hours and patients on anti-coagulant therapy. Convenient sampling method was applied to select the 108 eligible participants for the study.

Written informed consent was obtained from the legally eligible relative and re-consent was taken from the patient on return of consciousness. qSOFA score [14] was calculated at the time of admission for all patients with Decompensated Chronic Liver Disease patients and presumed infection. The parameters of

qSOFA score are Respiratory rate ≥22/ min, change in mental status, systolic blood pressure ≤ 100 mm/Hg with each score of 1. Participants with a qSOFA score ≥ 2 was considered as sepsis and included in the study. qSOFA score was a validated tool with the accuracy of 73.3% and specificity of 81.1% [15]. A pre-tested, content validated semi-structured questionnaire was used to collect the demographic data, clinical data, laboratory parameters, investigation information's and outcome of the participant. On the day of admission, the Prothrombin time-Albumin Ratio (PTAR) score was calculated to classify the participants as Low risk group (PTAR < 0.54), Medium risk group (PTAR 0.54 to < 0.82) and High-risk group (PTAR ≥ 0.82). The participants were treated appropriately as per the European Association for the Study of the Liver (EASL) guidelines and followed up for their outcome (Discharged/ Expired) until their duration of stay in the hospital. Then outcome was assessed for different risk categories classified by PTAR score.

Data entry was made in MS EXCEL 2019 and analysed using IBM SPSS software version 21.0, Chicago, USA. Numerical variables were represented in Mean ± Standard deviation and categorical variable was represented in proportions. The Chi-square test/ fisher`s exact test was applied to find the association between PTAR score and treatment outcome, other factors. p Value less than 0.05 was considered as statistical significance.

Ethical clearance was obtained from the Institutional Ethical Committee before the start of the study (GHIEC/2022/149). Participants/ legally eligible relatives were informed about the study and written informed consent form was obtained. The confidentiality of the information collected was ensured by the principal investigator.

Results

Characteristics of the Study Participants:

Table 1. General Characteristics of Study Participants (N= 108)

Variable		**n (%)**
Age (in years)	≤ 45	44 (40.7)
	> 45	64 (59.3)
Gender	Male	105 (97.2)
	Female	3 (2.8)
Smoking Addiction	Present	7 (6.5)
	Absent	101 (93.5)
Alcohol Addiction	Present	103 (95.4)
	Absent	5 (4.6)
Glasgow Coma Scale score	15	47 (43.5)
	<15	61 (56.5)

Duration of hospital stay	<7 days	64 (59.3)
	≥ 7 days	44 (40.7)
Treatment Outcome Status	Discharged	70 (64.8)
	Expired	38 (35.2)

Around 108 participants were recruited based on the eligibility criteria. The mean age of the study participants was 49.48 ± 11.28 (years) with age distribution in the range of 26- 87 (years). The proportion of the participants more than 45 years were 64 (59.3%). Majority of the participants were males 105 (97.2%). The distribution of the addiction behaviour that includes smoking and alcohol among the study participants were 7 (6.5%) and 103 (95.4%) respectively. Of the 108 participants recruited 64 (59.3%) spent less than a week of hospital bed days. The mean duration of hospital stay was 6.33 (± 3.21) days with the range distribution of 2- 18 days. The treatment outcome status shows that around one-third of the participants 38 (35.2%) died and 70 (64.8%) were discharged alive (Table 1).

Figure 1, represents the symptomology of the study participants on the day of admission. Most of the participants had more than one symptom at presentation. Almost all the participants 108 (100%) had ascites. The second most common presenting symptom was breathing difficulty 69 (63.9%). This was followed by jaundice 67 (62%), altered sensorium 55 (50.9%) and dark urine 46 (42.6%). The least reported symptom was blood in stools. 3 (2.8%).

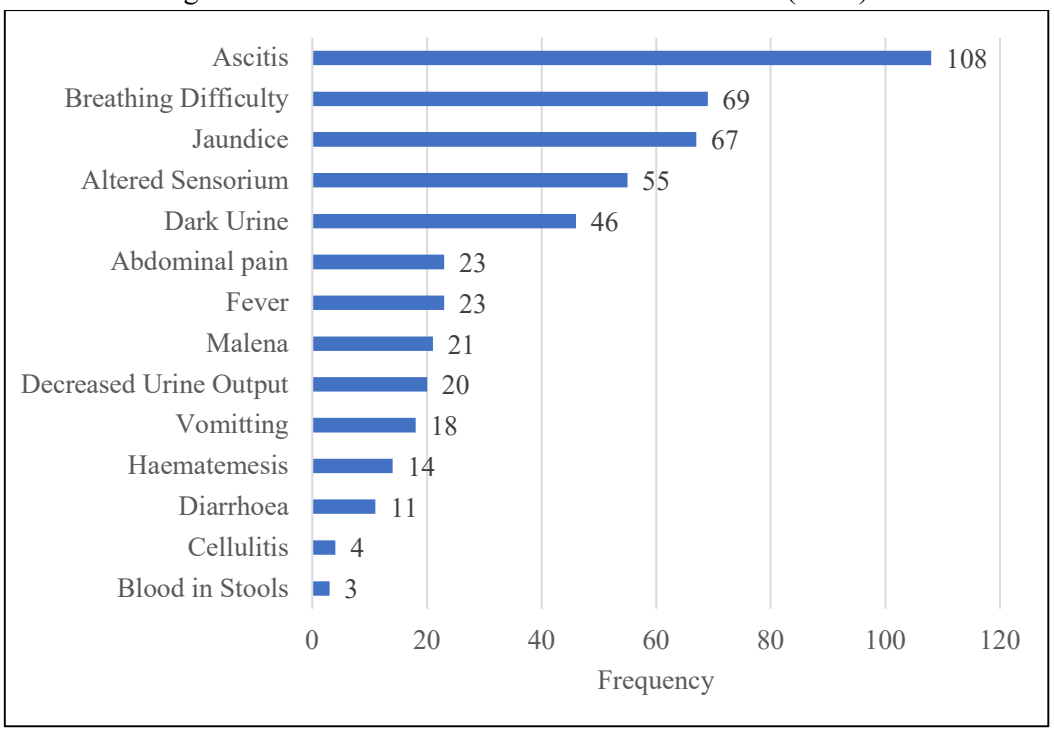


Figure 1. Distribution of Clinical Presentation at the Time of Admission (N=108). *Multiple responses type

Classification of patients based on PTAR

The quick Sequential Organ Failure Assessment (qSOFA) shows that majority of the participants 91 (84.26%) scored 2 and around 17 (15.74%) scored 3. The Prothrombin Time-INR to Albumin Ratio (PTAR) was used to risk categorize the study participants at the time of the admission and it shows that around one-third of the participants 39 (36.1%) and 38 (35.2%) were categorized as high risk and medium risk respectively and 31 (28.7%) of the participants were classified as low-risk group (Figure 2).

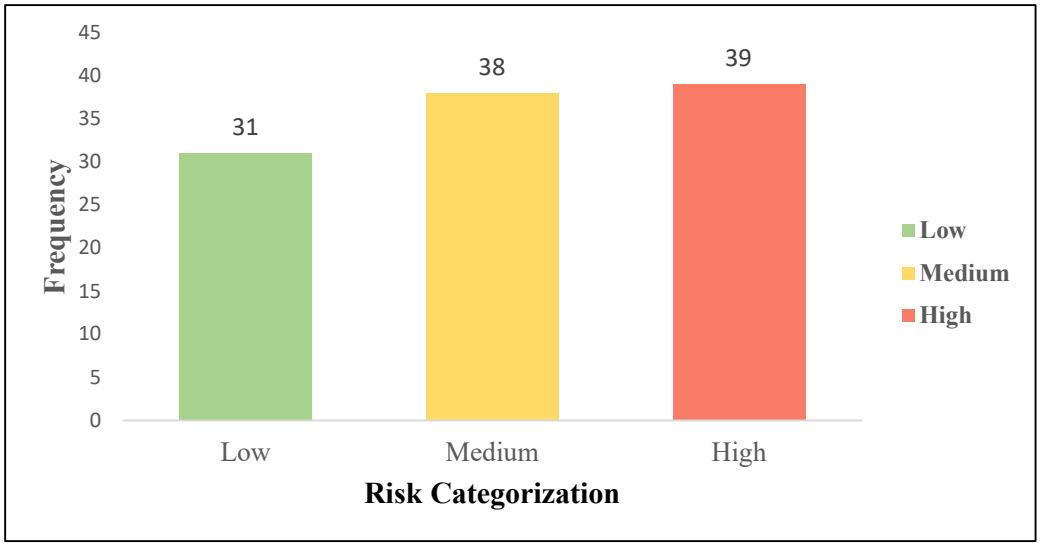


Figure 2. Risk classification of Study Participants based on PTAR (N=108)

Association between PTAR Risk Categorization and treatment outcome:

Table 2. Association between PTAR Risk Categorization and Treatment Outcome Status

Outcome Status	Expired	Discharged	**Chi-Square Value**	**p Value***
High Risk	24 (61.5)	15 (38.5)	18.59	0.000
Medium Risk	11 (28.9)	27 (71.1)		
Low Risk	3 (9.6)	28 (90.3)		

*Chi-Square test

The number of participants expired in the high-risk group was more than half 24 (61.5%) compared to only less than one-tenth 3 (9.7%) in the low-risk group. Vice versa, the proportion of participants discharged were 90.3% in the low-risk group compared to only 38.5% in the high-risk group based on PTAR score risk categorization. Among participants in the medium risk group also the proportion of

participants discharged were more than the expired (71.1% vs 28.9%). These differences were found to be statistically significant (p Value 0.000). [Table 2]

Factors associated with the unfavourable treatment outcome

Table 3 shows that the proportion of participants with treatment outcome status 'expired' was nearly doubled (26.6% to 47.7%) when it was compared between the participants duration of hospital stay of less than 7 days with participants of hospital stay more than or equal to 7 days. Also, the proportion of participants expired increases with decrease in Glasgow Coma Scale score (23.4% vs 44.3%). Duration of hospital stay and level of consciousness are associated with treatment outcome status and these association were also statistically significant. The other factors that include age, gender, smoking and alcohol addiction behaviour of the study participants has no association with the treatment outcome status. (p Value >0.05)

Table 3. Association between General Characteristics and Treatment Outcome (N=108)

Factor		**Expired**	**Discharged**	**p Value**
Age	> 45	22 (34.4)	42 (65.6)	0.832#
	≤ 45	16 (36.4)	28 (63.6)	
Gender	Male	37 (35.2)	68 (64.8)	1.000*
	Female	1 (33.3)	2 (66.7)	
Smoking Addiction	Present	5 (62.5)	3 (37.5)	0.126*
	Absent	33 (33.0)	67 (67.0)	
Alcohol Addiction	Present	37 (35.9)	66 (64.1)	0.467*
	Absent	1 (20.0)	4 (80.0)	
Duration of hospital stay	≥ 7 days	21 (47.7)	23 (52.3)	**0.024#**
	<7 days	17 (26.6)	47 (73.4)	
Level of Consciousness	GCS (<15)	27 (44.3)	34 (55.7)	**0.024#**
	GCS (15)	11 (23.4)	36 (76.6)	

*Fisher`s Exact test, # Chi-square test

Discussion

Total 108 participants of decompensated liver disease who scored more than or equal to 2 in qSOFA scoring and fulfilled the eligibility criteria were recruited for the study. PTAR score was applied to risk categorize the patients and discharge status of all the participants were recorded. It was found 31 (28.7%) were in low risk, 38 (35.2%) in medium risk and 39

(36.1%) in high-risk group. The proportion of mortality observed among the study participants were 38 (35.18%) of which 24 (61.5%) were in high risk, 11 (28.9%) in medium risk and 3 (9.6%) in low-risk group.

The mean age of the participants reported to the hospital with decompensated liver disease was 49.28 ± 11.28 years. A study conducted in a tertiary care hospital of Nepal by Bhattarai et al. [16] by recruiting 754 decompensated cirrhotic patients also showed that the mean age of decompensated cirrhosis was 54 ± 11.51 years. Studies from Indian region of Kolkata (2014) and Assam (2016) by Ray et al. [17] and Bhattacharyya et al. [18] also revealed that the mean age of decompensated liver disease admitted in a tertiary care hospital is near to our findings of 48.4 years and 45.8±10.45 respectively. Decompensated liver disease typically manifests in middle age due to the cumulative effects of various risk factors that includes hepatitis virus infection, alcohol, and the progression of liver damage over time [19]. The comorbidities also play a key role such as diabetes, hypertension, and cardiovascular diseases, which can exacerbate liver damage and contribute to decompensation [19].

Our study findings reflect that incidence of decompensated liver disease is higher in male group (97.2%) compared to the female. This is well known and does not appear to be changing with years. This might be because of the variation in distribution of most common risk factor 'alcohol addiction' for decompensated liver disease between the gender. This fact was supported by the evidence from national wide survey (National Family Health Survey- 5) [20], of India that men aged 15 years and above who consume alcohol was 18.8% compared to the women aged 15 years and above who consumed alcohol was 1.3%.

The proportion of total mortality reported in this study was 35.2% on following 108 participants to the point of outcome (discharge/ expired). On comparison a similar proportion 35.4% was observed in a hospital-based study by Sreeraj et al. [12] among the participants of cirrhosis of liver with sepsis.

The PTAR score has been investigated for its prognostic value in patients with decompensated liver disease. In our study the mean PTAR score of participants who survived was 0.68 ± 0.38 and those who died at the end of treatment was 1.01 ± 0.48. On comparison, the study by Zhang et al. [21] (2022) in the China among HBV associated decompensated cirrhosis indicates the mean PTAR score for those who died was 0.58 (0.42-0.77) compared to those survived 0.45 (0.37-0.58). Similarly in the same geographical region another study by Cai er al. [11] in 2021 indicate the mean PTAR score among those who died was 0.62 (0.55- 0.82) higher than those who survived 0.43 (0.35-0.54). These evidences suggest that a higher PTAR score is associated with worse prognosis and higher mortality rates [11,21].

The mortality rate observed across different risk categories based on PTAR score was 61.5%, 28.9% and 9.6% among high risk, medium risk and low risk group respectively. This data indicates that the proportion of mortality was higher in high risk and gradually steps down as the category becomes medium and low risk. On comparison with the study by Sreeraj et al. [12] shows that mortality rate was 76.93%, 23.08% and 14.29% among the high risk, medium and low risk category respectively.

This trend was similar to our findings. The strengths of our study were first of this kind in South Indian population and it is a prospective study. The limitations are lack of dynamic observation of PTAR score progressively during the hospital stay, a single-centre hospital-based study and influence of comorbidities like diabetes, immunocompromised conditions in the outcome were not studied.

Conclusion

The proportion of mortality reported among decompensated liver disease patients with sepsis in our study was 35.1%. The risk of mortality increases with increase in PTAR score that is participants those classified as high-risk. The factors associated with unfavourable treatment outcome are longer duration of hospital stay and decreased level of consciousness. To conclude the PTAR was an accurate tool to predict the outcome status of the decompensated liver disease patients with sepsis. It is easily calculated and could help the physicians in early identifications of patients with high risk of mortality and plan an appropriate aggressive management

Ethical Approval

Ethical clearance was obtained from the Institutional Ethical Committee before the start of the study (GHIEC/2022/149).

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

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ORIGINAL ARTICLE

Adapting to Virtual Learning: Exploring Challenges Faced by College Students in Online Classes

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Abstract

Background: Against the backdrop of Covid-19 pandemic there was a major shift in the education system. There was a transformation from the routine conventional learning to online mode of education. This study aimed to determine the multifaceted challenges encountered by college students in adapting to online classes. **Methods:** This descriptive cross-sectional study was conducted among college students between October and November 2020 in Tamil Nadu. The questionnaire was developed using google forms and disseminated via online platforms owing to Covid-19 restrictions. Data was entered in MS Excel and analysed using SPSS 27. Categorical variables were summarised in the form of frequencies and percentages and continuous variables summarised as mean and standard deviation. Independent t test was used to find the significant association between the students' perceptions and levels of education. **Results:** There were 243 study participants. Mean age of the students was 20.58±1.61 years. Mean hours spent per day on gadgets was 6.32±3.02 hours. The mean of average hours spent in studying is 4.12±2.01 hours. 80.2% of the students reported health issues due to online classes. Independent t test showed that students in lower levels of education had difficulties in coping up with online classes, understanding difficulties and felt this would affect their performance. **Conclusion:** Students faced significant challenges due to technological barriers, lack of social interaction, and difficulty in maintaining motivation and focus. As a result, students grappled with heightened stress levels and academic performance concerns, highlighting the urgent need for innovative solutions and support systems.

Keywords: Covid-19, Online classes, Challenges, College students

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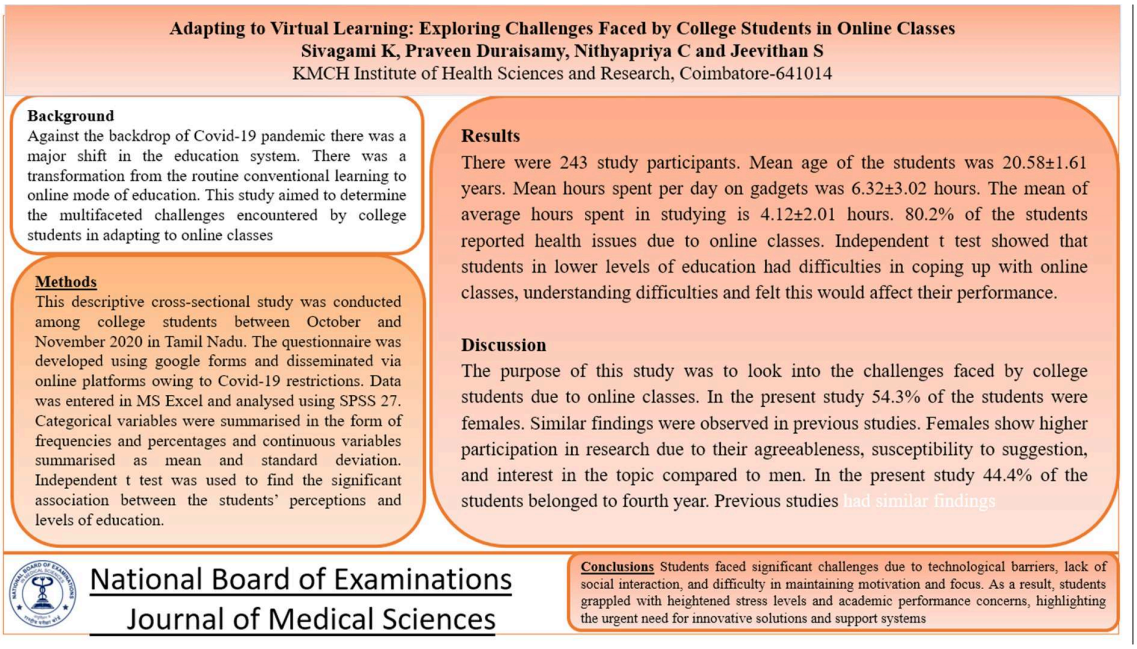
Graphical Abstract



Introduction

The WHO proclaimed Covid-19 to be a pandemic on March 11, 2020. The COVID-19 pandemic posed an unparalleled threat to food systems, public health, and the workforce. It had disastrous consequences on every facet of human existence. In order to reduce the transmission of disease lockdown was imposed which had an effect on many facets of human existence [1]. The impact on the educational system was unprecedented. Globally 600 million students and in India 320 million students were impacted [2].

Educational institutions had to shift to the new normal of online teaching due to this temporary closure [3]. There was a need to adopt innovative teaching for continuing education and to overcome mental stress and anxieties during the lockdown [4]. However, this transition was not without its hurdles, particularly for college students. Several factors affected the quality of online learning [3]. These include access to technical infrastructure and the quality of telecommunication network [3].

Students faced health issues attending continuous online classes. To raise the standard of instruction, it's critical to evaluate online learning from the viewpoint of the students. The purpose of this study was to determine the difficulties that students faced due to online learning. This was crucial for raising the calibre of online education and laying the groundwork for future instructional strategies that will be more successful.

Materials and Methods

The study, conducted between October and November 2020, surveyed college students in Coimbatore, Tamil Nadu, The data was collected using google forms due to Covid restrictions. The questionnaire consisted of 47 variables like the socio-demographic variables, presence of a suitable place for attending the classes, total hours spent on gadgets, primary gadget used for the online class, any additional

investment for the online classes, student's perception regarding online classes, health issues faced by the students due to online classes, advantages of online classes and the things missed by students due to online classes. Data was entered in Microsoft excel and analysed using SPSS 27. Categorical variables were summarised in the form of frequencies and percentages and continuous variables summarised as mean and standard deviation. Independent t test was used to find the significant association between the students' perceptions and levels of education. Ethical clearance was obtained with IEC number: 34/IHEC/2020.

Results

This study had 243 participants. The study population consisted of 243 participants, with a slight female predominance (54.3%) compared to males (45.7%). The majority of the students were from private colleges (97.5%), while only a small proportion (2.5%) were from government institutions. Regarding the course distribution, students from allied health sciences formed the largest group (35.4%), followed closely by engineering students (33.3%). Students from occupational therapy (12.3%), medicine (10.3%), and arts and science courses (8.6%) made up the remainder of the cohort. In terms of the year of study, fourth-year students constituted the largest proportion (44.4%), followed by third-year (24.7%), first-year (16.0%), second-year (13.2%), and a small number of fifth-year students (1.6%).

Nearly half of the students (46.9%) reported making additional investments to support their education during this period. Among these, mobile phones (51.0%) were the most commonly reported investment, followed by laptops (29.2%), new internet connections (12.5%), modems (7.9%), and furniture (5.7%) (Table 1).

Students across different years of study generally reported similar challenges with online learning, such as network issues, reduced attention span, and the need for greater self-motivation. However, significant differences were noted in specific areas. Students in earlier years (≤2 years) found it harder to cope without face-to-face faculty interaction (p=0.008) and required more time to understand web-based programs (p=0.02). In contrast, students beyond two years of study demonstrated better coping abilities (p=0.002), were more prone to distractions like observing friends during classes (p=0.002), and were more optimistic that their performance could improve with online learning compared to traditional teaching (p=0.003) (Table 2).

Table 1. Characteristics of the study participants (N=243)

Gender	**Frequency**	**Percent (%)**
Female	132	54.3
Male	111	45.7
College		
Private	237	97.5
Government	6	2.5
Course		
Allied health sciences	86	35.4
Engineering	81	33.3
Occupational therapy	30	12.3
Medicine	25	10.3
Arts and science	21	8.6
Year of study		
Fourth	108	44.4
Third	60	24.7
First	39	16.0
Second	32	13.2
Fifth	4	1.6
Additional investment	114	46.9%
Type of additional investment		
Mobile	58	51.0%
Laptop	33	29.2%
New connection	11	12.5%
Modem	7	7.9%
Furniture	5	5.7%

Table 2. Perceptions of online classes among students based on levels of education

Statements	**Year of study≤2 (Mean ± SD*)**	**Year of study>2 (Mean ± SD)**	**P-Value#**
Recurring network connectivity issues disturbs the classes	4.33±0.93	4.38±0.87	0.94
High speed internet facility is essential for uninterrupted classes	4.33±0.87	4.37±0.94	0.28
Continuous online sessions are academically very stressful	3.67±0.97	4.09±1.01	0.36

There is less chance for proper interaction with the faculty	3.50±1.02	4.00±0.91	0.56
Difficult to cope in the initial days	3.83±1.10	3.98±0.81	0.72
Without face-to-face interaction with teaching faculty learning is difficult	4.25±1.01	3.87±1.05	**0.008**
Difficulty in comprehension	4.13±0.94	4.06±0.89	0.62
Online class needs more self-motivation	4.04±0.94	3.85±0.87	0.13
Web based programs need lots of time for understanding	4.13±0.99	3.84±0.85	**0.02**
Reduced attention span	4.13±1.10	3.85±1.05	0.06
Unable to keep myself awake in post lunch sessions	3.93±1.13	3.91±0.94	0.87
Small group teaching and Focus group discussion facilitated learning better	3.94±0.90	3.71±0.89	0.06
Due to lack of supervision, I cannot resist myself from referring the text books during online	3.87±1.12	3.70±0.92	0.22
Switching off the cameras and microphones creates a better online environment	3.75±0.99	3.81±1.04	0.64
I don't find my home environment suitable for e-learning	3.76±1.16	3.71±1.16	0.75
I am unable to study after attending online classes	3.86±1.03	3.67±1.03	0.19
Ability to cope up with online class	3.27±1.10	3.66±0.81	**0.002**
More workload in online classes compared to regular classes	3.85±1.10	3.65±0.98	0.16
I have told I had some online issue when the faculty asked me a question	3.59±1.15	3.57±1.07	0.88
I sometimes see what my friends are doing in the online class	3.17±1.19	3.65±0.99	**0.002**
I don't have a separate calm room for online sessions	3.45±1.36	3.50±1.20	0.78
I am able to study well at home without any disturbance from friends/ classmates	3.11±1.21	3.26±1.10	0.35
Do you think your performance will increase with online teaching compared to traditional class room teaching?	2.48±1.27	2.98±1.14	**0.003**

*SD denotes standard deviation, # - Independent t test

Discussion

The purpose of this study was to look into the challenges faced by college students due to online classes. In the present study 54.3% of the students were females. Similar findings were observed in previous studies [1,5]. Females show higher participation in research due to their agreeableness, susceptibility to suggestion, and interest in the topic compared to men. In the present study 44.4% of the students belonged to fourth year. Previous studies had similar findings [6,7]. Higher education levels may increase survey engagement, as participants prioritize technical aspects and express more interest in expressing their viewpoints. Among the study participants 87% used mobile phones for online classes. Previous studies had similar findings [8,9]. Mobile devices are the most preferred technology due to their portability and ease of use.

Among the participants 80% faced health issues because of online classes. Previous studies had similar findings [10,11]. Students in the study experienced eye strain, dry eyes, headache, anxiety, and backpain due to increased screen hours, poor posture, and lack of physical activity. Among the participants 77% felt online classes stressful. Anger management issues were also brought on by endless internet activity [12]. Research indicates that students experiencing mental strain during online learning exhibit negative emotions such as anger, anxiety, fear, aggression, irritability, and frustration [13]. They might therefore gradually distance themselves from their loved ones.

Among the participants 86% faced difficulty in online classes due to internet connectivity issues. Previous studies showed similar findings [14,15]. The government and telecom providers should collaborate to improve internet and communication infrastructure for online learning. In case of academic disruptions, the Ministry of Education should provide more Android and iPhone devices for college students.

Most participants found online classes difficult to concentrate, found home environments unsuitable, and felt that online classes required significant self-motivation. Previous study by Bozkurt et al. [16] showed similar finding. In traditional classrooms, students found active engagement in academic activities easier due to direct teacher interaction and this helped on timely homework completion, preventing procrastination. The present study showed that small group discussions facilitated learning better. Previous study observed a similar finding [17]. Present study showed that 86% of the students reported to have missed the routine college life. Studies by Kedraka and Kaltsidis et al. [18] and Rameez et al. [19] also reported similar results. The study revealed that students in lower levels of education struggled with understanding online classes and perceived performance reduction compared to higher education students. Similar finding was observed in previous study [20]. Students in higher education levels may exhibit stronger self-control, reducing the disturbance caused by external videos, allowing individuals to maintain control over their learning behaviours.

Conclusion

College students face numerous challenges in online classes due to technical, logistical, and personal issues. These include unreliable internet connections, difficulty adjusting to virtual learning platforms, feelings of isolation, and blurring boundaries between home and

academic life. To overcome these challenges, a multifaceted approach involving technological infrastructure improvements, academic support services, and proactive measures is needed.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

Ethical Approval

Ethical clearance was obtained with IEC number: 34/IHEC/2020.

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ORIGINAL ARTICLE

An Observational Descriptive Study Regarding the Outcome of Retinopathy of Prematurity Screening in Tertiary Care

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Abstract

Background: Low birth weight, prematurity, and prolonged oxygen therapy are some of the variables that contribute to Retinopathy of Prematurity (ROP), a disorder that affects premature infants and can cause blindness owing to undeveloped retinal blood vessels. With rising neonatal survival rates, ROP incidence has increased. This Observation descriptive study aimed to identify risk factors, assess their relationship with ROP, and estimate its incidence in preterm newborns at our tertiary care center, considering both genetic and environmental influences. **Materials and Methods:** For two years, from May 2022 to May 2024, the Department of Ophthalmology at Chengalpattu Medical College & Hospital carried out this observation descriptive study. Sample size of around 1500- Low birth weight newborns (less than 2,500g) and preterm infants (less than 37 weeks) who were checked for ROP were included. Indirect ophthalmoscopy, a 20D lens, a portable fundus camera, Vectis, and a wire speculum were among the tools utilized. Inclusion criteria covered all intramural infants meeting gestational age or weight criteria, while exclusions included those with ocular media opacities or inadequate follow-up (<3 visits). Point estimates and 95% CI were computed using IBM SPSS Statistics 26.0 for data analysis. **Results**: Of the patients in our study, the majority (98.9%) had no ROP, whereas 0.5% had stage 1, 0.5% had stage 2, and 0.1% had stage 3. 52.1% of the 1500 newborns were male, and 47.9% were female. The following risk factors were shown to be significant by univariate analysis: low gestational age, low birth weight, RDS, PDA, sepsis, NEC, and blood transfusion; there were also substantial correlations between PDA and blood transfusion. Low birth weight was validated by multivariate logistic regression as an independent risk factor for ROP. **Conclusion**: This study emphasizes low birth weight and PDA as key independent risk factors for ROP, highlighting the need for targeted neonatal care, PDA prevention, and cautious blood transfusion practices. The findings align with existing research, reinforcing the importance of comprehensive neonatal management. Future studies should explore early biomarkers and intervention strategies to further reduce ROP incidence and improve outcomes for preterm infants.

Keywords: ROP, Risk Factors, Low Birth, Neonatal Care

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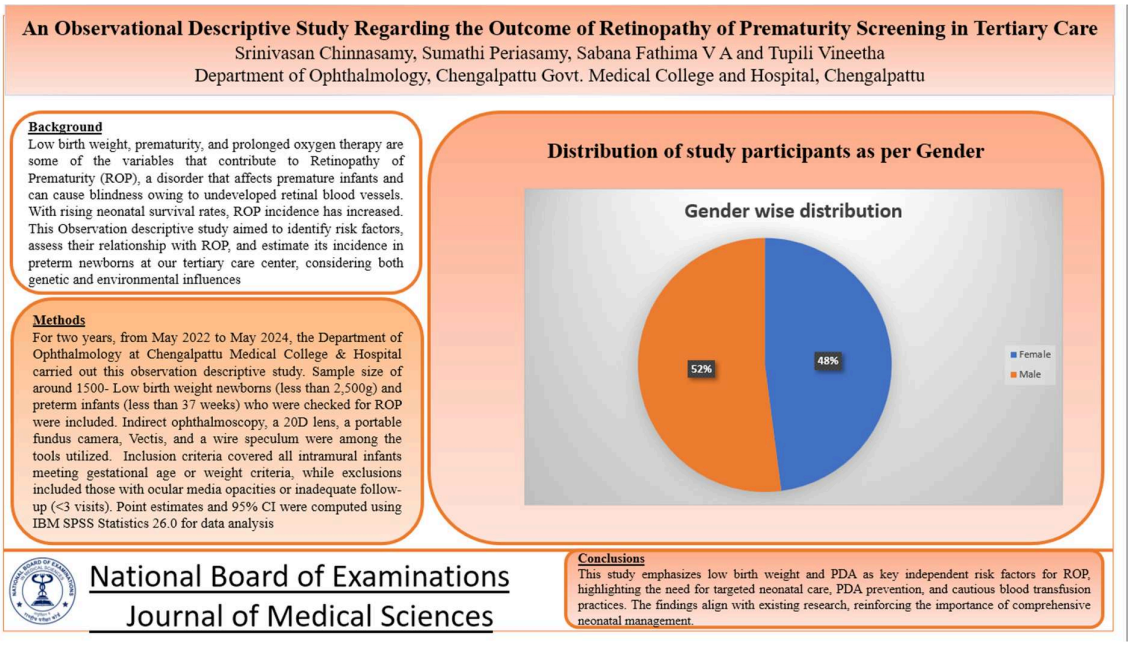
Graphical Abstract



Introduction

Retinopathy of prematurity (ROP) is a significant cause of preventable blindness worldwide, particularly affecting premature infants. The World Health Organization (WHO) has highlighted ROP as an emerging cause of childhood blindness, especially in middle-income countries such as Latin America, Eastern Europe, India, and China [1]. Geographical disparities play a crucial role in the prevalence and severity of ROP, with low-resource settings experiencing higher rates due to limited access to adequate neonatal care [2]. ROP primarily affects the developing retinal vasculature of preterm infants. The disease spectrum ranges from mild forms, which often resolve spontaneously without causing significant visual impairment, to severe forms characterized by pathological neovascularization. Blindness and retinal detachment may result from these severe cases if treatment is not received. Extremely preterm infants, especially those delivered before 25 weeks of gestation, now have higher survival rates thanks to advancements in neonatal care [3]. However, because these infants are more likely to acquire ROP, the increased prevalence of the ailment has coincided with this improved survival [4].

Premature babies are the main victims of the multifactorial condition known as retinalopathy of prematurity (ROP). Low birth weight (BW), low gestational age (GA), and concomitant diseases including intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), and patent ductus arteriosus (PDA) are among the risk factors that have been found. Long-term exposure to more oxygen has also been linked to the development of ROP. Extremely low birth weight (ELBW) and extreme prematurity further elevate the risk of severe ROP [5]. Early detection and timely intervention are critical to prevent the progression of ROP and its associated complications. Historically, transscleral cryotherapy was

employed to ablate the avascular retina, significantly reducing adverse anatomical and visual outcomes in threshold and pre-threshold ROP, as demonstrated by the Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) trial. However, cryotherapy was associated with considerable postoperative inflammation and discomfort [6]. Subsequently, transpupillary laser photocoagulation emerged as a preferred treatment modality, offering better visual outcomes, a reduced likelihood of inducing myopia, and faster disease regression compared to cryotherapy. Laser therapy also presented advantages such as decreased postoperative morbidity, less stress to ocular tissues, easier access to the posterior pole, and a reduced need for general anesthesia [7].

Anti-vascular endothelial growth factor (VEGF) medicines, like bevacizumab, have been investigated as possible therapies for ROP in more recent years using intravitreal injections. These agents target pathological neovascularization and have shown promise in managing severe cases of ROP. However, concerns regarding potential systemic side effects and the long-term safety profile of anti-VEGF therapy necessitate further investigation [8]. Long-term and consistent follow-up is essential to monitor disease regression or progression and to identify and manage associated morbidities, including myopia, anisometropia, amblyopia, and strabismus. Despite efforts to emphasize timely ROP screening and educate families on the necessity of follow-up, reports evaluating the effectiveness of ROP screening programs remain limited [8]. This observation descriptive study aimed to quantify the frequency of ROP in preterm neonates at our tertiary care center, identify the risk factors that predispose to ROP, and assess the association between ROP and its risk variables.

Material and Methods

This study is an Observation descriptive study, conducted in our Department of Ophthalmology, Chengalpattu Medical College & Hospital. The study period 2 year from May 2022-May 2024. All preterm <37 week and low birth weight <2500g infants who were screened for ROP. Sample size =1500The materials used in this study was wire speculum and Vectis, indirect ophthalmoscopy and 20 D Lens portable fundus camera. The inclusion criteria in our study we include all intramural baby who were less than 37 weeks of Gestational age and /or had a birth weight less than 2500g were examined. Infants were excluded from the study if they had ocular media opacities that interfered with fundus examination. Patient who did not complete the follow up less than minimum of 3 visits examination was excluded from the analysis. In our study all patients who were enrolled in the study were examined. Pupils were dilated using plain tropicamide eye drops diluted with lubricant at least 30 min prior to examination. Topical anesthetic agent applied and eye speculum inserted. Fundus were examined using indirect ophthalmoscopy with 20D LENS. A lubricant was used during examination.

If ROP is detected, to verify the zone, stage, and extent of ROP, detected fundus photography was taken. The Revised International Classification of ROP was used to categorize retinalopathy of prematurity. Both the presence and absence of plus disease and ROP were noted. GA, BW, maternal and newborn risk factors, such as sepsis, apnea, necrotizing

enterocolitis, intravenous hemorrhage, and outcome, were among the data that were documented. Until retinal vascularization was finished, screening tests were conducted. if any ROP stages were found. Until retinal vascularization was finished, screening tests were conducted. if any ROP stages were found. In order to enter and evaluate data, IBM SPSS Statistics version 26.0 was utilized. 95% CI and a point estimate were computed. Multivariate logistic regression analysis (Table 1).

Results

Table 1. Distribution of study participants as per ROP stage wise

STAGES	Frequency	Percent
STAGE 1	7	0.5
STAGE 2	7	0.5
STAGE 3	2	0.1
No ROP	1484	98.9
Total	1500	100.0

The above table shows the distribution of study participants as per ROP stage wise. Among our study participants about 0.5% were belong to stage 1, 0.5% were also belong to stage 2. About 0.1% were belong to stage 3. Majority of about 98.9% does not have any ROP (Figure 1).

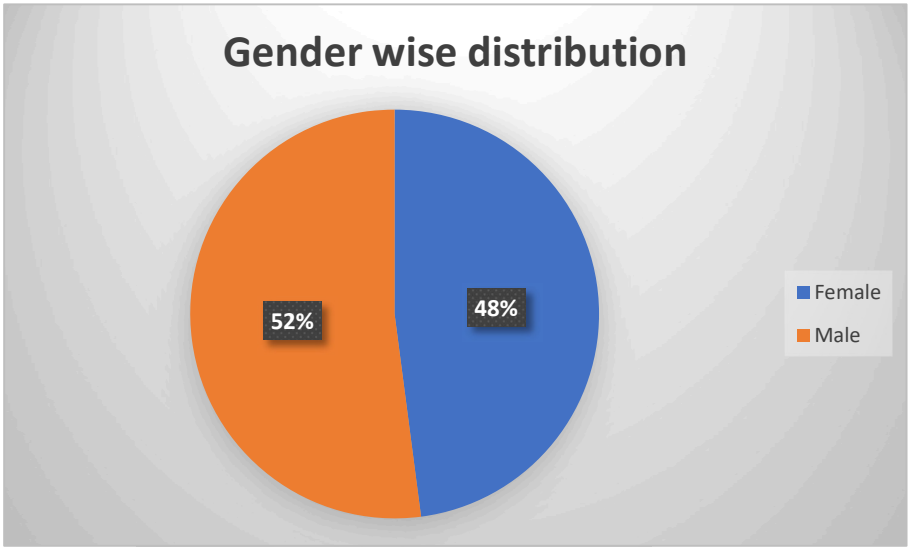


Figure 1. Distribution of study participants as per Gender.

The distribution of study participants by gender is depicted in the above figure. 781 (52.1%) and 719 (47.0%) of the 1500 newborns were male and female, respectively (Table 2).

Out of 1500 babies 233(15.53%) were ≤32 weeks of gestational age and 1267 (78%) were between 32 and 37 weeks (Table 3).

Table 2. Distribution of study participants as per Gestation age

Age at Gestation (WKS)	Frequency	Percent
≤32WKS	233	15.53
32-37WKS	1,267	84.47
Total	1,500	100.00

Table 3. Univariate risk factors for the onset of any severity of retinopathy of prematurity in 1500 screened newborns

Risk Factors	Odds ratio	95% confidence interval	P value
Age of low gestation (days)	1.325	1.124 -1.942	0.032
low weight at birth (g)	1.674	1.0485-1.198	0.045
RDS	6.485	1.003-24.684	0.002
PDA	10.716	4.742-48.127	0.001
SEPSIS	5.781	0.671-10.853	0.004
NEC	4.125	0.942-12.412	0.012
IVH	2.378	0.438-5.813	0.945
BLOOD TRANSFUSION	10.831	3.279-45.687	0.002

The retinopathy of prematurity (ROP) development risk variables for 1,500 examined newborns are displayed in the above table. Low birth weight, respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), sepsis, necrotizing enterocolitis (NEC), low gestational age, and blood transfusion were all found to be significant risk factors by univariate analysis. The associations between PDA (OR: 10.716, p = 0.001) and blood transfusion (OR: 10.831, p = 0.002) were especially strong. Nevertheless, there was no significant correlation between intraventricular hemorrhage (IVH) and ROP (p = 0.945) (Table 4).

Table 4. Multivariate logistic regression studies of risk factors for the occurrence of any severity of retinopathy of prematurity in 1500 screened newborns

Risk factors			
Age of low gestation (days)		Multivariate logistic modalities were excluded.	
low weight at birth (g)	1.0043	1.002-1.0092	0.0051
RDS		Multivariate logistic modalities were excluded.	
PDA	4.894	1.039-25.784	0.0472
SEPSIS		Multivariate logistic modalities were excluded.	
BLOOD TRANSFUSION		Multivariate logistic modalities were excluded.	

Table 4 demonstrates that only low birth weight (OR: 1.0043, p = 0.0051) and PDA (OR: 4.894, p = 0.0472) remained independently significant risk factors for ROP after confounding factors were adjusted for using the multivariate logistic regression model. Other variables such as low gestational age, RDS, sepsis, and blood transfusion were excluded from the final model, suggesting their effects may be confounded by other factors rather than acting as direct independent predictors. This indicates that while multiple factors contribute to ROP, low birth weight and PDA play the most critical independent roles. Identifying and addressing these factors, particularly through improved neonatal care and management of PDA, could be essential in reducing the risk of ROP in preterm infants.

Discussion

From our study it had been found that the majority of the infants (98.9%) did not develop retinopathy of prematurity (ROP), with only a small percentage classified into various stages of ROP: Stage 1 (0.5%), Stage 2 (0.5%), and Stage 3 (0.1%). This low incidence of ROP contrasts with findings from other studies, such as Kocabeyoğlu et al. [9], who reported an ROP prevalence of 21.72% in preterm infants. The variation in ROP prevalence could be due to differences in neonatal care, oxygen therapy practices, and screening protocols across different healthcare settings. With regarding to the gender distribution of the study participants was nearly equal, with 52.1% male and 47.9% female infants. Previous studies have shown conflicting evidence regarding the role of gender in ROP development. Some reports suggest a slight male predisposition due to differences in fetal lung maturity and oxidative stress responses, but many studies, including this one, found no statistically significant association between gender and ROP risk by Fleck et al. [10]. From our study, it had observed that 15.53% of infants were born at or before 32 weeks, while 84.47% were born between 32 and 37 weeks. Prematurity

remains one of the strongest risk factors for ROP due to incomplete retinal vascularization at birth. Studies by Sundar et al. [11] support this finding, emphasizing that earlier gestational age significantly increases ROP risk due to prolonged exposure to supplementary oxygen and immature vascular development.

A number of significant risk factors were found by the univariate analysis, including blood transfusion, respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), sepsis, necrotizing enterocolitis (NEC), low birth weight, and short gestational age. The strongest associations were found with PDA (OR: 10.716, p = 0.001) and blood transfusion (OR: 10.831, p = 0.002). These findings align with research conducted by Shah et al., which identified PDA and blood transfusion as major contributors to ROP due to increased exposure to oxidative stress and hemodynamic instability by Shah et al. [13]. The Multivariate Logistic Regression Analysis of Risk Factors for ROP Development shows after adjusting for confounding factors, only low birth weight (OR: 1.0043, p = 0.0051) and PDA (OR: 4.894, p = 0.0472) remained independently significant risk factors for ROP. Other factors such as low gestational age, RDS, sepsis, and blood transfusion were excluded, suggesting their effects were mediated through other variables. These results are supported by studies from the Early Treatment for Retinopathy of Prematurity Cooperative Group, which also found that low birth weight was the most robust predictor of ROP progression a per Titawattanakul et al. [14].

Conclusion

This study underscores the importance of low birth weight and PDA as independent risk factors for ROP. The findings highlight the need for targeted interventions, including optimizing neonatal care, preventing PDA-related complications, and minimizing unnecessary blood transfusions. Future research should focus on early biomarkers and intervention strategies to further reduce ROP incidence and improve outcomes for preterm infants. These conclusions align with existing literature and reinforce the critical role of comprehensive neonatal care in mitigating ROP risk.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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CASE REPORT

Open Anterior Component Separation (ACS) for Complicated Incisional Hernia

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Abstract

This study looks open anterior component separation (ACS) followed by placement of an onlay mesh for complicated incisional hernia surgery. Among surgical procedures incisional hernia surgery is most complex as it involves repairing of weakened abdominal muscle which can be due to preexisting conditions, sudden increase in intra abdominal pressure, straining during motion or while lifting heavy objects. In this case patient presented with an incisional hernia with a very bad scar after two major exploratory laparotomy. We have chosen anterior component separation over posterior component separation due to ease of operation, less surgical time and early recovery. Evidence from long-term studies suggest that the use of mesh helps to strengthen the muscular wall of the abdomen and organ deformation is prevented. In conclusion, anterior component separation with onlay mesh repair is established technique for hernia repair surgery.

Keywords: Mesh hernial repair, incisional hernia, onlay mesh, synthetic mesh

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Introduction

Incisional hernia is a weakness or bulge in the abdominal wall at the site of previous surgical incision. This is more common with midline incisions. Hernias can be of different types and sizes, either a small or a big bulge. Despite surgical techniques the incidence of the incisional hernia is still between 15% to 20% [1].

The European Hernia Society (EHS) has classified midline incisional hernias by dividing them into 5 zones, M1 to M5, based on their location:

- M1: Sub xiphoidal, from the xiphoid to 3 cm below
- M2: Epigastric, from 3 cm below the xiphoid to 3 cm above the umbilicus
- M3: Umbilical, from 3 cm above to 3 cm below the umbilicus
- M4: Infraumbilical, from 3 cm below the umbilicus to 3 cm above the pubis
- M5: Suprapubic, from the pubic bone to 3 cm above

In this case hernia involved 3 zones i.e. M2, M3 and M4. The repair of incisional hernias can be done surgically by various techniques from which we opted for onlay mesh repair with ACS. It involves covering the abdominal wall fascial defect with a mesh. When this method is compared to conventional methods such as suture repair, the mesh repair method stands out and also significantly reduces greatly the chance of recurrence by providing support and a scaffold for tissue healing [2].

Case report

A 24 year old male patient came with chief complaint of swelling around umbilicus since 1year which was gradually progressive and associated with pain. Patient had a history of two exploratory laparotomy in past 3year. On examination the swelling extended from the epigastric region to the infraumbilical region measuring approximately 16x8cm, while the scar approximately 18x9cm. No other history of medical comorbidity. Ultrasonography confirms the defect size through which omental fat and bowel are seen herniating. Rest of organs finding were normal.

An incision was made along the scar margin, and the scar was excised. Thorough and extensive bowel adhesiolysis was performed. The subcutaneous plane was created laterally up to the anterior axillary line on right side and upto linea semilunaris on left side. Then on left side external oblique aponeurosis was incised just laterally to linea semilunaris from the subcostal region superiorly to the anterior superior iliac spine inferiorly. Then a space was created between external and internal oblique muscles at the mid axillary line on left side. Mesh fixation was performed in the created plane, followed by a tension-free closure (Figure 1).

Figure 1. Measuring the hernia defect (Length and Breadth).

Discussion

Anterior Component Separation remains an operation plagued by high surgical morbidity. Separation of the abdominal wall components involves significant subcutaneous undermining from midline to the level of semilunar line in order to achieve exposure of the external oblique. The mesh was used to help in repairing the abdominal wall defect. The mesh was attached with the help of sutures along the tissue line of the defect [3]. In the present scenario, synthetic mesh i.e., polypropylene mesh was used. The prolene mesh is made up of a nonabsorbable polymer which has a higher tensile strength even when compared to the other mesh. It is light weight, non-polar and does not degrades making it one of the most commonly used mesh in hernioplasty [4].

Common complications are the logical sequelae of large myofascial and subcutaneous flap elevation and include seroma, hematoma, infection, skin edge necrosis, wound breakdown and hernia recurrence, Recurrence rate following anterior component separation range from 5 to 32% in major series and rate of wound complications range from 7.5 to 48% [5].

Separation of abdominal components has become an essential and powerful weapon among surgeons across specialities, gaining widespread popularity for the closure of abdominal wall defects resulting from trauma, infection and previous surgery. This has been applied to various problems, consistently yielding reproducible results (Figure 2).

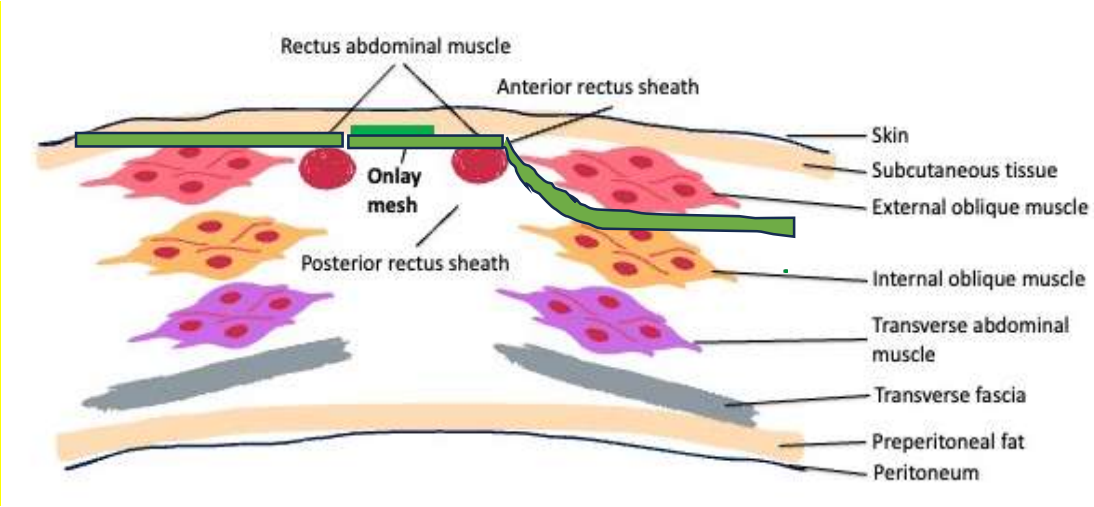

Figure 2. Placement of an onlay mesh.

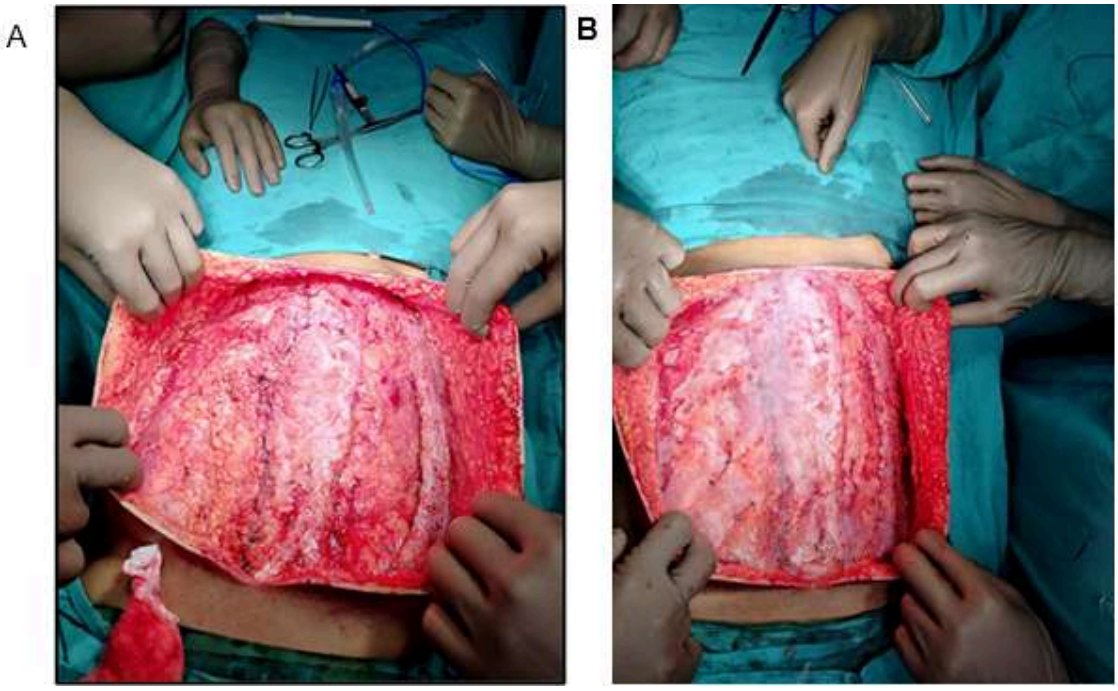

Figure 3. Incision made upto peritoneum (a) and image taken after placement of mesh (b).

This approach is straightforward, reliable, and preserves the midline structures. Following the procedure, the patient experienced an uneventful recovery and was discharged on POD 15th with noticeable improvement in pain and swelling.

Conclusion

One of the most effective ways to manage complex incisional hernia is using open anterior component separation (ACS) technique along with onlay mesh repair. This surgical technique provides a reliable option for addressing large and complex

hernias while significantly reducing the chances of recurrence and morbidity.

Conflict of Interest

All the authors state that they do not have any conflict of interest.

Ethics approval

Not required.

Consent for publication

For the publication of this case report, written and informed consent was obtained from the patient.

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CASE REPORT

Pilonidal Sinus Over Nasal Dorsum: Incidental Finding

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Abstract

Pilonidal refers to a collection of hair. The pilonidal sinus is a subcutaneous track containing hairs or their microscopic fragments. The sinus penetrates into the subcutaneous layers as a bulbous diverticulum with or without branching side channels. The presence of a hair tuft in the sinus cavity or tract is the characteristic feature of the pilonidal sinus. We describe the case of a 13-year-old paediatric patient in this case study who developed a chronic, intermittently discharging sinus tract on the dorsum of the nose, Magnetic resonance imaging (MRI) of PNS showed a localized blind subcutaneous tract over the dorsal aspect of nose. A tiny area of abnormal signal intensity along the dorsal aspect of lower 1/3rd of nose reaching upto skin surface, however no obvious intranasal cavity opening or aspirable pocket or collection noted, possibly sinus tract. The patient has a presence of a sinus tract over the dorsum of nose; surgery was performed with exploration of the sinus by injecting methylene blue dye which subsequently facilitated a precise excision, ensuring complete removal of the sinus, through external *rhinoplasty* approach. Histopathological analysis revealed a sinus tract lined with keratinized stratified squamous epithelium containing a tuft of hair, patient was followed up for three months; without any complaint of any complication or recrudescence.

Keywords: Pilonidal sinus, unusual sites, atypical locations, Sinus tract, Nasal dorsum

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Introduction

One typical issue with the anorectum is pilonidal disease that primarily affects younger individuals, typically found in age group of 15 to 40 years. It is caused by shed hair which are drawn into the subcutaneous tissue. Hair can become damaged due to friction, leading to breakage, this can result in the hair entering through the open mouth of the sweat gland or penetrating the softened skin, which may occur due to sweat or dermatitis. The typical symptoms include pain and discharge. The nature of pain can range from dull ache to throbbing pain. Discharge can vary from a minimal amount of fluid to a sudden outpouring of pus.

Pilonidal sinus, mostly occur in the sacrococcygeal region, but it can also occur across various anatomical sites. Cases involving nasal structures, such as the nasal bridge and preauricular region, highlight the diverse clinical spectrum of this condition [1-4]. Furthermore, reports of pilonidal sinus in unusual sites like the umbilicus, interdigital spaces, give evidence that this ailment can occur anywhere in the body with hair follicles [4,8]. It can occur in hairdressers, dog groomers, jeep drivers and sheep shearers which shows that it is an occupational disease [5]. This review aims to synthesize the diverse array of reported cases, shedding light on the evolving understanding of pilonidal sinus manifestations across the human body.

Case Report

A 13-year-old paediatric male patient, has presented to our outpatient clinic with complaint of discharging sinus on nasal bridge. The intermittent discharge over the past four years suggests a chronic inflammatory process, possibly indicative of a sinus tract.

A very small visible opening was present over the lower part of nasal dorsum. There was absence of palpable swelling or discharge upon examination which poses a diagnostic challenge, emphasizing the importance of imaging studies. The magnetic resonance imaging (MRI) findings suggestive of a tiny area of abnormal signal intensity of size 2.8mm × 3mm noted along dorsal aspect of lower 1/3rd part of nose reaching upto skin surface, however no obvious intranasal cavity opening or aspirable pocket of collection noted, possibly sinus tract.

Surgical excision of sinus was done under general anaesthesia by giving a midline incision over the nasal dorsum starting from the sinus opening (Figure 3). The intraoperative tracing of the sinus tract with dye injection facilitated precise excision, ensuring complete removal of the sinus through dissection from the neighbouring tissues (Figures 1 and 2). Closure of the cavity was done in two layers. On cutting & opening the sinus we found that there was a tuft of hair, present inside the sinus wall.

The sinus was then sent for histo-pathological examination. The specimen was identified as a pilonidal sinus which confirmed the diagnosis. No new complaints developed during the post-operative and follow-up period (Figure 4).

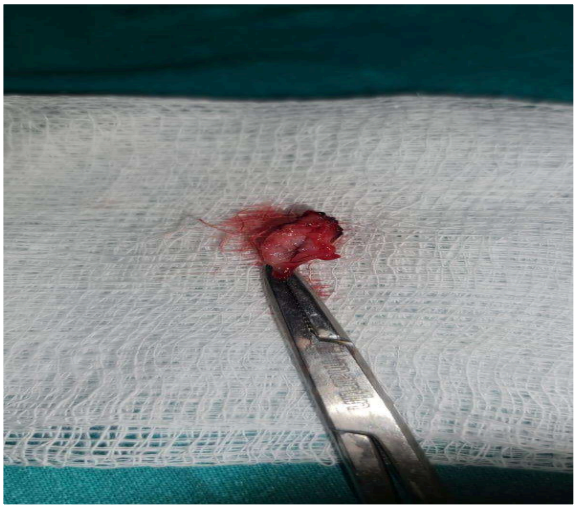

Figure 1. The Specimen shows an epithelial lined sinus tract with a tuft of hair.

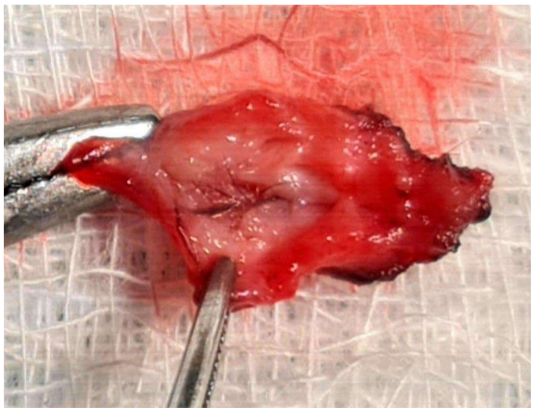

Figure 2. Specimen of Excision of Sinus.

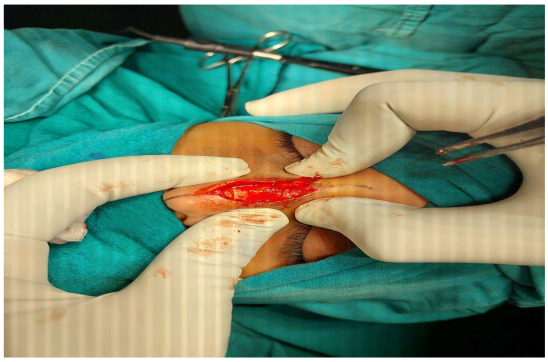

Figure 3. Intra operative image of nasal dorsum.

Figure 4. Clinical photograph of patient on follow up after 1 month.

Discussion

A condition known as the pilonidal sinus is present in the natal cleft situated above the coccyx, include of one or more, typically uninfected, midline openings, which connects with a fibrous track that is lined by granulation tissue and consisting of loose hair in the lumen. The pilonidal sinus is mainly composed of 3 contents; granulation tissue, epithelial scars and debris and dead hairs which may resting loosely in the sinus, situated within granulation tissue and deep within the developed scar tissue [6,7]. It is mainly occur in dark haired hirsute man, obese male and in individuals whose occupations typically linked to friction and shearing forces [9,10]. These risk factors are not present in our patient.

While many patients show no symptoms, a few of the patient establish pain, local infection, discharge and hyperaemia. The complications of pilonidal sinus include recurrent inflammation, abscess formation and recurrence of sinus [11]. Recurrence is probably due to the inadequate excision, entry of new hair through the scar or skin.

Management modalities vary depending on factors such as the site of involvement, disease severity, recurrence, patient comorbidities, cosmetic concerns and patient preferences [12]. While surgical excision remains the definitive management in many cases [13]. Abscess formation requires drainage of the pus or fluid present in the sinus tract lumen.

Furthermore, the role of patient education and lifestyle modifications helps in prevention of pilonidal sinus disease. Encouraging measures such as regular hygiene practices, weight management, and avoidance of prolonged sitting, friction movements may reduce the likelihood of recurrence. Further research should be done to explore the aetiology and management strategies for pilonidal sinus in atypical locations like the nasal dorsum.

Conclusion

Pilonidal sinus disease includes a range of symptoms, diagnostic difficulties, and treatment options. More research is needed to better understand the condition, improve diagnosis, and develop better treatment plans. Pilonidal sinus in the nasal area, like in our case, is very uncommon.

Statements and Declarations

Conflict of interest

In relation to the research, writing, and publication of this work, the authors hereby affirm that they possess no conflict of interest.

Ethics approval

Informed consent for publication was obtained from the parents and The Institutional Ethics Committee gave their approval to the case review.

Competing interests

Authors declare that they have no competing interests.

Funding

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SHORT COMMUNICATION

Three Cases of Brain Tumor in Pregnancy

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Abstract

Background: Brain tumours in pregnancy are a pathology that carries risk to both maternal and fetal health. It is considered a case of interest in the point of surgical management. **Objective**: The literature reviewed to show the effect of pregnancy on these tumours, the diagnosis and management. **Methods**: 3 cases were reported to the institution which was managed with the multidisciplinary approach which has been mentioned. **Conclusions**: The presence of a brain tumour associated with pregnancies implies a high risk of maternal and perinatal morbidity and mortality requiring multidisciplinary management and a treatment team with surgical experience

Keywords: Meningioma, pregnancy, glioma

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Introduction

Pregnancy alone causes significant physiological changes in women. The existence of an intracranial tumour during pregnancy can lead to major consequences, such as increased maternal mortality [1]. Managing a central nervous system (CNS) tumour during pregnancy involves numerous problems. According to population-based studies, brain tumours are linked to an increased risk of maternal mortality, preterm birth, intrauterine growth restriction (IUGR), and cesarean delivery [2]. The incidence of brain tumours in pregnant women is believed to be 1 in 1000-2000 pregnancies, and it is comparable between pregnant and non-pregnant women. Malignant brain tumours occur in 3.6 out of every 1 million live births [3]. According to the literature, the most common primary tumours include gliomas, meningiomas, pituitary adenoma, and metastases from breast carcinomas [4]. Pregnant women are at higher risk of developing brain tumours due to changes in their anatomy and physiology. Cerebellar granular cells have been reported to have an effect when their estrogen receptors are stimulated. In predisposed women, the emergence and growth of tumors may therefore be influenced by the correlation with the elevated levels of this hormone noted during pregnancy. The presence of tumor cellular receptors, including estrogen and progesterone receptors, EGFR, FGF 2, PDGFR B, and VEGF, has been directly associated with increased levels of hormones and growth factors and the progression of intracranial tumours [5]. Pregnancy causes an increase in the volume of maternal blood, which may contribute to edema surrounding the tumor and enhance regional cerebral blood flow. Headache, nausea, vomiting, neurologic symptoms, and seizures are examples of symptoms of elevated intracranial pressure that may mimic early pregnancy symptoms or pregnancy-related hypertension disorders like eclampsia or pre-eclampsia. Based on existing research, brain tumour-induced repetitive seizures affect 27–41% of expectant mothers. The mass effect is the primary cause of brain tumour symptoms [6,7]. Seizures and other neurologic symptoms may worsen during pregnancy in people who already have gliomas, and these symptoms may cause obstetric crises. Elevated vascularity of tumours like gliomas because of hormonal fluctuations may be connected to an increase in intracranial tension (ICT). Acoustic schwannomas, meningiomas, gliomas, and brain metastases from breast cancer are examples of hormonally driven tumours that may grow more quickly during pregnancy due to changes in hormone levels [8].

Case 1

A 24-year-old female patient presented with a history of headaches for 4 months which was maximum during the morning hours, associated with vomiting, imbalance, and blurring of vision. There was no history of trauma, loss of consciousness, convulsion or limb weakness. She was hypothyroid, hypertensive, and had arthritis. She was in the 30^{th} week of gestation. On clinical examination, vitals were stable with GCS (Glasgow Coma Score) of 15 (E4V5M6), pupils were equal and reacting to light, visual acuity was diminished in both eyes with the presence of double vision, and

gaze evoked nystagmus on lateral gazes. Motor system examination revealed normal power in all 4 limbs, with a normal sensory system. The right plantar was extensor and left equivocal with reduced tone. Knee jerks were pendular. She was unable to walk without support. Romberg's sign was positive, with eyes open, where she was swaying to both sides. Ultrasonography revealed a live fetus of 30 weeks. She was planned for expectant management till more fetal maturity. MRI brain (Figure 1) showed T1 hypointense lesion, T2 flair iso to hyperintense to grey matter and DWI showed diffusion restriction in a large posterior fossa mass, associated with hydrocephalus. She underwent an emergency VP shunt initially for obstructive hydrocephalus and later went for an elective posterior fossa craniotomy and excision of the infratentorial tumor with duroplasty, followed by a Lower Segment Caesarian Section (LSCS) to deliver the healthy but premature baby (32 weeks) in the same sitting. She had a good recovery, with a modified Rankin scale of 2. Histopathological examination (HPE) of the tumour was suggestive of medulloblastoma and IHC (Immuno-Histo-Chemistry) showed synaptophysin patchily positive, Ki67- 60%, ATRX- Positive, P53- wild type, beta catenin- membranous and cytoplasmic positive, CD45, GFAP, S100 – negative, all of which confirmed it to be an Anaplastic Medulloblastoma. She was advised Chemotherapy and Radiotherapy.

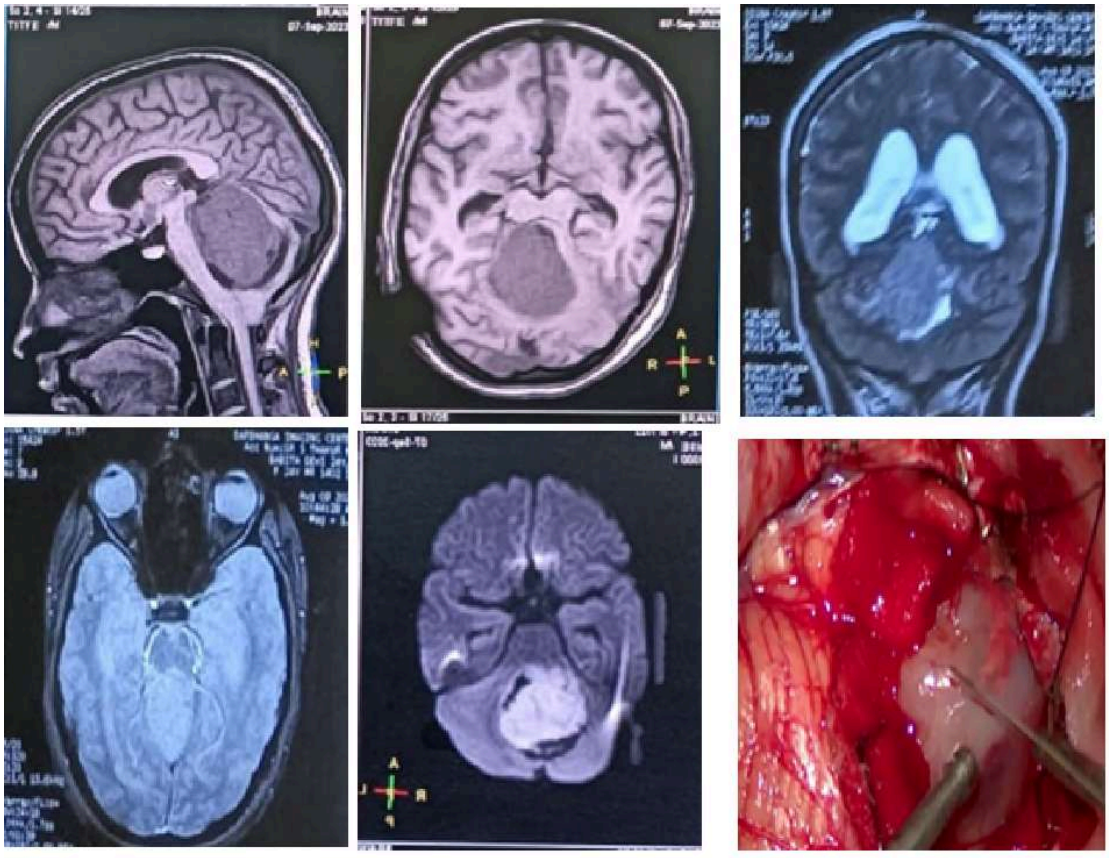

Figure 1- MRI images Showing medulloblastoma and Intra-op images

Case 2

A 35years old female patient presented with headache and blurring of vision in the left eye for 15 days. On examination, she had mild dysphasia, and had a right-sided pronator drift. Abdominal examination revealed a live fetus of 36 weeks of gestation. MRI brain showed (Figure 2) large solid T1 hypointense and T2 hyperintense extra-axial lesion in the left temporal region, most likely a meningioma, originating from the greater wing of the sphenoid causing compression on the left lateral ventricle causing significant mass effect. She underwent elective LSCS and a left craniotomy for the tumour in the same sitting. Histopathological Examination was suggestive of chordoid meningioma. On IHC, GFAP was positive, EMA stain showed diffuse membranous staining in tumour cells, PR receptor showed diffuse strong nuclear straining, P53 was the wild type, Ki67 of 12% all of which were suggestive of an Atypical meningioma (Gr 2, WHO). She is under regular follow-up with MRI surveillance. A 3-month contrast MRI didn't show any residual or recurrent tumour.

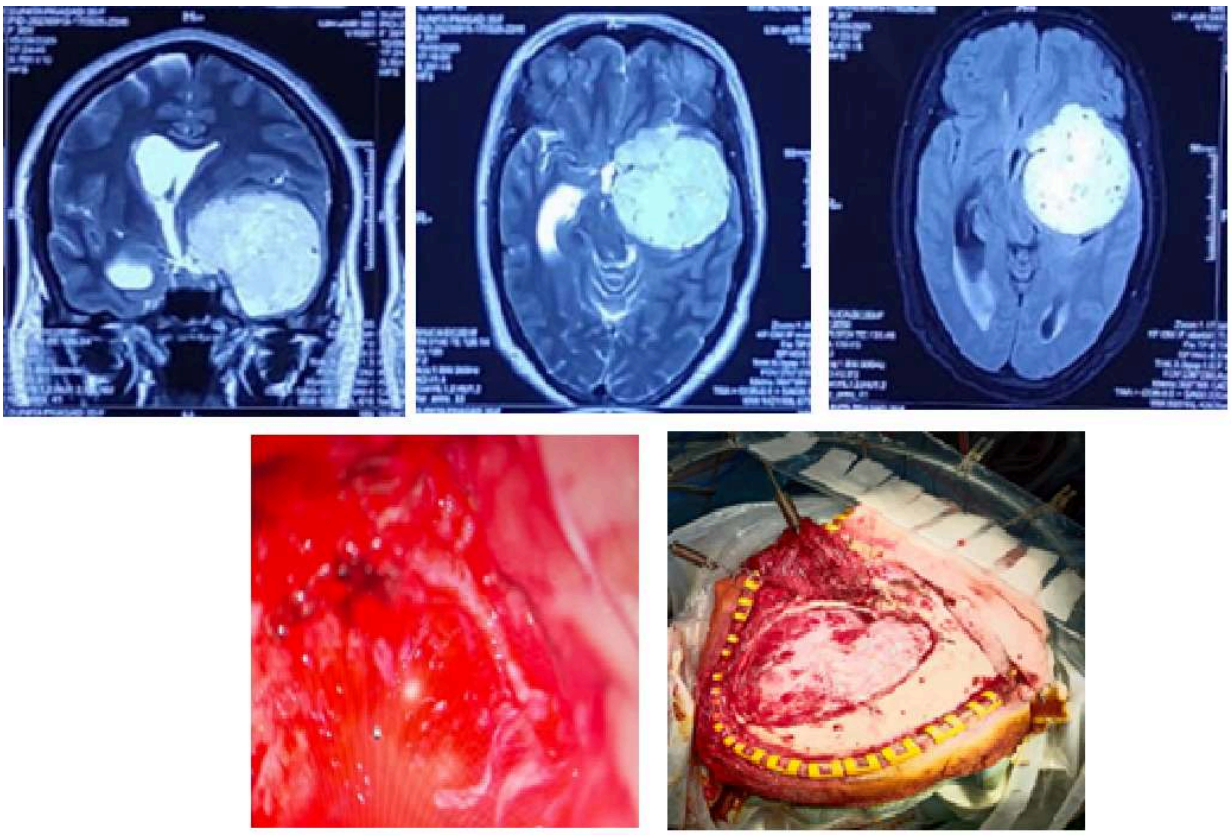

Figure 2. MRI Shows Meningioma originating from the greater wing of the sphenoid (above) and intraop images(below)

Case 3

A 34-year-old female presented with visual disturbances in both eyes for 1 month associated with headache and giddiness for the same duration. She was 6 months pregnant. On further evaluation, her vital parameters were in the normal range. She was blind in the left eye, and in the right, only perception of light was present. On Fundoscopy, bilateral papilloedema was present with secondary optic atrophy. MRI Brain (Figure 3) showed a T2 hyperintense intra-axial lesion in the left parietal-occipital-temporal region compressing over the left lateral ventricle, suggestive of a low-grade glioma. She underwent neuro-navigation-guided craniotomy and excision of the brain tumour, which was uneventful. HPE of the tumour showed a Diffuse Glioma (WHO grade 2) - NOS and was advised IHC IDH Mutant, CDKN2A/B Retention. The fetal monitoring was done during the tumour surgery and later LSCS was performed at 36 weeks

Figure 3. MRI Images showing Diffuse Low-Grade glioma over left parieto-temporal region.

Discussion

The biggest challenge regarding the treatment of brain tumours diagnosed during pregnancy is the timing of surgery. In our study, in 2 patients the fetus was delivered at the same sitting with the excision of the tumour and in one patient the tumour was excised with postoperative fetal monitoring to allow further fetal maturity. Caesarean section was preferred in all patients to avoid increased intracranial pressure from vaginal delivery and difficulty of vaginal delivery due to the immaturity of the cervix in preterm labour.

Medulloblastoma is a malignant brain tumor (WHO grade IV) formed by stem cells in the cerebellum's sub-ependymal matrix or external granular layer [9]. The care of medulloblastoma during pregnancy is a difficult decision since the mother's and fetus's well-being must be balanced against the hazards of treatment. An early delivery should be considered because the outcome may not be positive. A tumor that causes brainstem compression is an emergency. Any delay may imperil both the mother's and the fetus' lives [10].

Meningiomas are believed to account for between 13% and 26% of all cerebral

tumors [11]. The abundant expression of progesterone receptor (PR) in meningiomas is well recognized. The evidence that several meningiomas enlarge and become symptomatic in pregnancy and reduce in size after delivery suggests an important role of the hormone [12]. In a study of 17 gestational meningiomas, Lusis et al. found that hemodynamic changes during pregnancy, increased blood volume, and vascularization all contributed to the tumors' rapid growth. In contrast to other types of meningiomas, gestational meningiomas exhibit intra- and extracellular oedema, as well as typical foamy, swollen cells. Pregnancy is characterized by significant hormonal swings, which may result in growth or symptom exacerbations. Therefore, it is possible that an undiagnosed meningioma was already present prior to pregnancy, causing a rise in its size [13].

Diffuse low-grade gliomas (LGGs) are intra-axial, World Health Organization grade II neoplasms that account for approximately 7% of adults' primary central nervous system tumours [14]. Yust-Katz et al [15] summarized MD Anderson's experience with gliomas of different grades in pregnancy and observed that among women who became pregnant after glioma diagnosis and harboured grade II&III tumours, 44% had confirmed tumour progression during pregnancy or within 8 weeks of delivery.

Conclusion

The symptoms of co-existing brain tumours are usually masked by the symptoms of pregnancy. There may be a relationship between pregnancy hormones and the rate of brain tumour growth mediated through specific intracellular receptors. Finally, when considering treatment modalities and timing of surgery for the tumour, each patient should be managed through a multidisciplinary approach based on a personalized treatment algorithm.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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PERSPECTIVE

Professional Exodus among Medicos: A Matter of Concern

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Abstract

The phenomenon of sudden professional dropout from the medical field is a multifaceted issue influenced by personal, systemic, and societal factors. Physicians and healthcare workers face unparalleled demands, including prolonged work hours, emotional exhaustion, and significant responsibility, which often contribute to burnout and work-life imbalance. The overwhelming academic pressure, parental and social expectations, limited opportunities at elite medical universities, job market challenges and economic inequality, high living costs and unattainable aspirations, rebellion against the work culture**,** disillusionment with social mobility and the influence of social media and pop culture lead to professional exodus

Keywords: Professional exodus, Burnout, Involution, Chokubi phenomenon, rotting

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Professional exodus is a metamorphosis that can happen at any time – during student days while working as a junior doctor or as a postgraduate student. Good and sincere medicos suddenly snap up, get tired of the rat race, and simply give up. In every batch of MBBS students, there will be some who keep on failing in semester exams and end up completing their 5-year MBBS course in 10 or more years, that too when their examiners get truly merciful. They have embraced this lifestyle of simply giving up and making no effort to improve their performance by studying, attending classes and clinics, and discussing their difficulties with teachers, or classmates. This is also not typically an Indian phenomenon, in recent years, a growing number of young people in China have been embracing this lifestyle which they call ‘bai lan’, or "let it rot." This term reflects a mindset of giving up on societal expectations and opting out of the traditional rat race. It follows the earlier Chinese attitude called "tang ping," or "lying flat," a movement, where individuals chose minimalism and rejected overwork. The term bai lan, refers to the act of willingly stepping back from chasing certain goals after realizing they are simply too challenging to accomplish.

This trend of "rotting" among youth is a reaction to mounting societal pressures and economic challenges. This lifestyle reflects a conscious decision to give up on traditional success markers and societal expectations. A study found Internal medicine and family practice physicians accounted for more than 16,000 of the 71,309 doctors who left the field by 2022 [1]. Another study from Puerto Rico found that the island lost 46 % of doctors in 13 years [2]. There can be many causes of this

1. Overwhelming Academic Pressure

Our education system is one of the most competitive in the world, and young people often face immense stress from a very young age. 10-1200,000 students appear for JEE and only 10,000 get selected in 23 IITs of India. The NEET 2023 statistics show that there were 20,38,596 examinees out of 20,87,462 registered candidates for 41,388 government medical college seats and 76,928 private seats [3]. Students spend years in preparation, often sacrificing social lives and personal growth. For many, failing to excel can feel like a permanent setback, leaving them disillusioned and burned out.

2. Parental and Societal Expectations

Indian parents often place immense pressure on their children to succeed academically, viewing education as the primary pathway to upward mobility. This high-stakes environment creates a "sink or swim" mentality.

3. Limited Spots at Elite Medical Universities

With millions of students competing for a small number of spots at top-tier medical universities, many feel they are stuck in an unforgiving system that rewards only a select few. For those who fail to meet these expectations, embracing "rotting" can be a way of rejecting the unrealistic demands placed on them. The National Eligibility cum Entrance Test-Post

graduation (NEET PG) 2024 saw a total of 2,16,136 candidates appearing from 416 centers spread across 170 cities in 31 states for just 70,645 postgraduate seats.

4. Job Market Challenges and Economic Inequality

Even for those who excel academically, the transition to the workforce presents its own set of hurdles.

(a) Hyper-Competitive Job Market: Medical College graduates often find themselves competing for a shrinking pool of desirable jobs in government hospitals or in corporate hospitals. Many are left underemployed or working in jobs far below their qualifications. Those with overseas university degrees find it even more difficult to compete. This leaves many young people feeling pessimistic about their future prospects.
(b) Rise of "Involution": This is a term that has gained popularity in China, and it describes a situation where individuals are forced to work harder without achieving meaningful progress or rewards [4]. There is not enough value for the effort they are putting in. Many workers feel trapped in a cycle of overwork and diminishing returns. These economic pressures lead many young people to adopt "rotting" as a form of silent protest or a way to cope with the frustration of an unfair system.
(c) Economic inequality: When medical graduates look back at their schoolmates, and find that those who fared poorer than them academically, and could not get through the tough medical entrance test, are faring much better economically and enjoying a better-quality life, they feel frustrated and disillusioned. This can be the inception of ‘rotting’.

5. High Living Costs and Unattainable Aspirations

Young doctors are increasingly finding it difficult to achieve traditional milestones of success, such as owning property, starting a family, or building a stable career due to compensation dissatisfaction [5].

(a) Skyrocketing Housing Prices: In major cities like Delhi, Mumbai, Bangalore and Chennai real estate prices have soared, making homeownership virtually unattainable for many young people. The high cost of living adds further strain.
(b) Cultural Norms and Family Pressure: In Indian culture, owning property and achieving financial stability are often prerequisites for marriage. Many young doctors feel unable to meet these expectations, leading to frustration and disengagement.
(c) Delayed Life Milestones: As a result of these pressures and wanting to achieve more in life, more young doctors are delaying marriage and parenthood, choosing instead to focus on their immediate personal needs or simply opting out of the system altogether. The rotting" mindset can be seen as a rejection of the societal narrative that links happiness and self-worth to material achievements.

6. Rebellion against the Work Culture

Junior doctors in India have no fixed working hours, and duty hours can often stretch to 36 hours with very little relaxation time in between. This has faced increasing backlash in recent years about the workplace culture due to the health care worker shortage [6].

(a) Exhaustion and Burnout: Overcrowded government hospitals and busy corporate hospitals demand grueling work hours, leaving junior doctors with little time or energy for personal pursuits. Burnout is rampant, leading these young doctors to question whether such sacrifices are worth it.
(b) Limited Rewards for Hard Work: Despite their best efforts in an understaffed hospital, many doctors feel they are not adequately compensated. Stagnant wages, coupled with rising living costs, create a sense of futility.
(c) Cultural Shift: The younger generation of doctors are increasingly unwilling to prioritize work over their well-being. They are challenging the older generation's emphasis on self-sacrifice and instead embracing a mindset of self-care and minimalism. "Rotting" represents a rebellion against this toxic work culture, prioritizing mental health and personal contentment over relentless ambition.

7. Disillusionment with Social Mobility

The promise of upward mobility—a cornerstone of India's economic boom in previous decades—now feels out of reach for many junior doctors. They feel their classmates from school, who chose other professions, are earning much more, and the exalted stature that the doctor once had in society is also not to be seen, particularly if one is not economically well off.

(a) Income Inequality: The wealth gap in India has widened significantly. Young doctors from middle- and lower-income families often feel that their chances of improving their socioeconomic status are slim if they do not get a good consultant position.
(b) Perceived Futility: With societal structures favoring the wealthy and well-connected, many feel that hard work and talent are no longer enough to succeed in the medical world.
(c) Generational Differences: Previous generations grew up in a time when there was enormous respect and reverence for doctors. Today’s doctors face a much more stagnant and uncertain landscape. Physical violence and verbal aggression against them are common as the newer generation of patients are prepared to spend money but expect a guaranteed cure. Faced with these realities, "rotting" offers a way to disengage from what feels like an inherently unfair system.

8. Influence of Social Media and Pop Culture

Social media platforms like WhatsApp, Facebook and X have amplified the "rotting" mindset, allowing young doctors to share their frustrations and form communities.

(a) Collective Identity: Online forums provide spaces where individuals can commiserate and validate each other's feelings of disillusionment, normalizing the choice to "rot."
(b) Satirical Content: Memes, videos, and other content mocking societal pressures have become hugely popular, spreading awareness of movements like "bai lan" and "lying flat" (tang ping).
(c) Cultural Heroes: It is trendier to be Munnabhai MBBS than a serious doctor in social media. The rise of minimalist lifestyles in pop culture—such as characters who reject societal norms—has also inspired young people to question traditional paths to success.

9. Impact of the COVID-19 Pandemic

The pandemic has accelerated disillusionment among India's young doctors. They had risked their lives and helped the country to fight the pandemic with the sincerity of soldiers guarding the frontiers of our country, but they feel they were not duly rewarded. They now have time to reflect on their lives and question their priorities. Was it worth risking our lives for a society of people who still abuse us at the flimsiest pretext, they wonder. This introspection often led to a reevaluation of societal norms. Those young doctors who had started new practices felt the economic brunt of unpaid mortgages and are yet to recover from it. The pandemic also shone a spotlight on the importance of mental health, prompting many to prioritize their well-being over external achievements.

The Way out of the problem

This attitude of giving up and rot is very dangerous and potential threat to economic growth and social stability. In Japan, the aging population, low birth rates, and economic pressures is forcing young physicians to choose non-insured aesthetic medicine immediately after their mandatory 2-year residency, thereby bypassing further training in other specialties, a phenomenon known as 'Chokubi phenomenon' [7]. Efforts are urgently required to address the underlying issues, such as implementing policies aimed at reducing work hours and promoting mental health awareness and government appreciation of the junior doctors for their contribution to fighting the Covid pandemic. A preferential selection for post-graduate degree or diploma courses may be very encouraging. Workplace security and stringent government laws for the safety and security of junior doctors and a secure and safe working environment for them is mandatory.

The "rotting" phenomenon among our young doctors is a multifaceted response to the immense academic, economic, and cultural pressures they face. It reflects a broader reevaluation of values, with the younger generation starting to prioritize personal fulfillment, mental health, and work-life balance that makes sense to them over the traditional markers of success. While it has not yet sparked concern among older generations and the government, "rotting" highlights a growing demand for systemic change in our social and economic structures. Only the future will tell if that change is coming in this burnout and

stressed toxic culture for the medical fraternity.

Authors Contribution

Conception and design of the study – SB, NB; Acquisition of data- SB, NB, NB; Drafting of the article – KB, NB, NB, SB; Critical revising – SB, NB; Final approval- KB, NB, NB, SB

Statements and Declarations

Conflicts of interest

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