GASTRIC INSUFFLATION WITH HIGH FLOW NASAL CANNULA OXYGEN THERAPY IN PATIENTS ADMITTED IN ADULT INTENSIVE CARE UNIT: AN OBSERVATIONAL STUDY

THESIS

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

DOCTOR OF MEDICINE (MD)

(ANAESTHESIOLOGY AND CRITICAL CARE)

JUNE 2022 **DR ANJANA RAMACHANDRAN**

AIIMS, JODHPUR

DECLARATION

I hereby declare that the thesis titled "GASTRIC INSUFFLATION WITH HIGH FLOW NASAL CANNULA OXYGEN THERAPY IN PATIENTS ADMITTED IN ADULT INTENSIVE CARE UNIT: AN OBSERVATIONAL STUDY" embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

Dr Anjana Ramachandran

Department of Anaesthesiology and Critical Care,

All India Institute of Medical Sciences,

Jodhpur

All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled "Gastric insufflation with High Flow Nasal Cannula Oxygen Therapy in patients admitted in Adult Intensive Care Unit: An Observational Study " is the bonafide work of Dr. Anjana Ramachandran

carriedout under our guidance and supervision in the Department of Anaesthesiology and CriticalCare, All India Institute of Medical Sciences, Jodhpur.

Guide

Dr. Pradeep Bhatia
Professor and Head
Department of Anaesthesiology & Critical Care
AIIMS Jodhpur

Co-Guides

Dr. Manoj Kamal
Additional Professor
Department of Anaesthesiology & Critical Care
AIIMS Jodhpur

Dr. Sadik Mohammed
Associate Professor
Department of Anaesthesiology & Critical Care
AIIMS Jodhpur

Dr. Swati Chhabra
Associate Professor
Department of Anaesthesiology & Critical Care
AIIMS Jodhpur

Dr. Bharat Paliwal
Associate Professor
Department of Anaesthesiology & Critical Care
AIIMS Jodhpur

CERTIFICATE

This is to certify that the thesis titled "Gastric insufflation with High Flow Nasal Cannula Oxygen Therapy in patients admitted in Adult Intensive Care Unit: An Observational Study" is the bonafide work of Dr Anjana Ramachandran carried out under our guidance and supervision in the Department of Anaesthesiology and Critical Care, All India Institute of Medical Sciences, Jodhpur.

Dr. Pradeep Bhatia

Professor and Head

Department of Anaesthesiology and Critical Care

AIIMS, Jodhpur

ACKNOWLEDGEMENT

"Success is not the key to happiness. Happiness is the key to success. If you love what you are doing, you will be successful"

-Albert Schweitzer

First and foremost, I am deeply grateful, and it is my proud privilege to express my deep sense of gratitude and sincere thanks to my thesis guide Dr. Pradeep Kumar Bhatia, Professor and Head, Department of Anaesthesiology and Critical Care, AIIMS, Jodhpur who provided me with an opportunity to work under his guidance. His guidance was paramount in providing a well-rounded experience and knowledge. He has always been a source of encouragement and inspiration. I wish to express my deep in debt gratitude for devoting his valuable time out of his busy schedule and being concerned for the completion of this project. I shall remain grateful to him forever.

I would also wish to express my sincere gratitude to Dr. Manoj Kamal, Additional Professor,

Department of Anaesthesiology & Critical Care, AIIMS Jodhpur, Dr. Sadik Mohammed, Associate Professor, Department of Anaesthesiology & Critical Care, AIIMS Jodhpur, Dr. Swati Chhabra, Associate Professor, Department of Anaesthesiology & Critical Care, AIIMS Jodhpur and Dr. Bharat Paliwal, Associate Professor, Department of Anaesthesiology & Critical Care, AIIMS Jodhpur for their constant support, encouragement, guidance and help throughout my work.

I am also extremely thankful to my colleagues Dr. Sangamala Venkata Prem Kumar, Dr. Markandey Prasad, Dr. Shipra Roy, Dr. Somya Goel, Dr. Priyadarsan M, Dr. Anas VP with whom I worked closely and puzzled over many similar problems. I am very grateful for their presence during my difficult times. A special thanks to my seniors Dr. Nilay Pal, Dr. Balakrishna, Dr. Samarth Agarwal and Dr. Arunima Mohan for their constant motivation and support. I extend my gratitude to all my amazing juniors and my seniors at the Department of Anaesthesiology and Critical Care, AIIMS, Jodhpur for their selfless help during my day-to-day work.

Most importantly, I would like to thank my family for providing me with unfailing support andcontinuous encouragement throughout my years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them.

My warm appreciation is due to all the Anaesthesiology staff and technicians who cooperated in my long working hours. At last, words are short to express my heartfelt appreciation to all the participants who willingly and selflessly participated in my thesis during my research endeavour.

Dr. Anjana Ramachandran

INDEX

ABBREVIATIONS

HFNC	HIGH FLOW NASAL CANNULA
HFNO	HIGH FLOW NASAL OXYGEN
FIO_2	FRACTION OF INSPIRED OXYGEN
CPAP	CONTINUOUS POSITIVE AIRWAY PRESSURE
COT	CONVENTIONAL OXYGEN THERAPY
NIV	NON-INVASIVE VENTILATION
CT	COMPUTED TOMOGRAPHY
AIIMS	ALL INDIA INSTITUTE OF MEDICAL SCIENCES
AP	ANTERO-POSTERIOR
APD	ANTERO-POSTERIOR DIAMETER
TV	TRANSVERSE
TVD	TRANSVERSE DIAMETER
ACSA	ANTRAL CROSS-SECTIONAL AREA
GV	GASTRIC VOLUME

SpO_2	OXYGEN SATURATION BY PULSE OXIMETRY
ABG	ARTERIAL BLOOD GAS
PaO_2	PARTIAL PRESSURE OF OXYGEN
SaO_2	ARTERIAL OXYGEN SATURATION
$PaCO_2$	PARTIAL PRESSURE OF CARBON DIOXIDE
ARF	ACUTE RESPIRATORY FAILURE
ICU	INTENSIVE CARE UNIT
RR	RESPIRATORY RATE
HR	HEART RATE
SBP	SYSTOLIC BLOOD PRESSURE
DBP	DIASTOLIC BLOOD PRESSURE
MBP	MEAN BLOOD PRESSURE
MMHG	MILLIMETRES OF MERCURY
NHF	NASAL HIGH FLOW
HFFM	HIGH FLOW FACE MASK

PEEP	POSITIVE END EXPIRATORY PRESSURE
PES	ESOPHAGEAL PRESSURE
SARS-COV-2	SEVERE ACUTE RESPIRATORY SYNDROME- CORONAVIRUS 2
O_2	OXYGEN
COPD	CHRONIC OBSTRUCTIVE PULMONARY DISEASE
EADI	ELECTRIC ACTIVITY OF DIAPHRAGM
CM H2O	CENTIMETRE OF WATER
MINS	MINUTES
USG	ULTRASONOGRAPHY
L	LITRE
ML	MILLILITRE
USCSA	ULTRASONOGRAPHIC MEASUREMENT OF GASTRIC ANTRAL CROSS-SECTIONAL AREA TO PREDICT GASTRIC VOLUME
IEC	INSTITUTIONAL ETHICS COMMITTEE
CTRI	CLINICAL TRIALS REGISTRY INDIA
ROC	RECEIVER OPERATOR CHARACTERISTIC CURVE

MHZ	MEGAHERTZ
CM	CENTIMETRE
MM	MILLIMETRE
D1	ANTERO-POSTERIOR DIAMETER
D2	LONGITUDINAL DIAMETER
SPSS	STATISTICAL PACKAGE FOR THE SOCIAL SCIENCES
IQR	INTERQUARTILE RANGE
KG	KILOGRAM
BMI	BODY MASS INDEX
DM	DIABETES MELLITUS
CAD	CORONARY ARTERY DISEASE
IHD	ISCHEMIC HEART DISEASE
HTN	HYPERTENSION
CKD	CHRONIC KIDNEY DISEASE
CI	CONFIDENCE INTERVAL
BPM	BEATS PER MINUTE
P VALUE	PROBABILITY VALUE

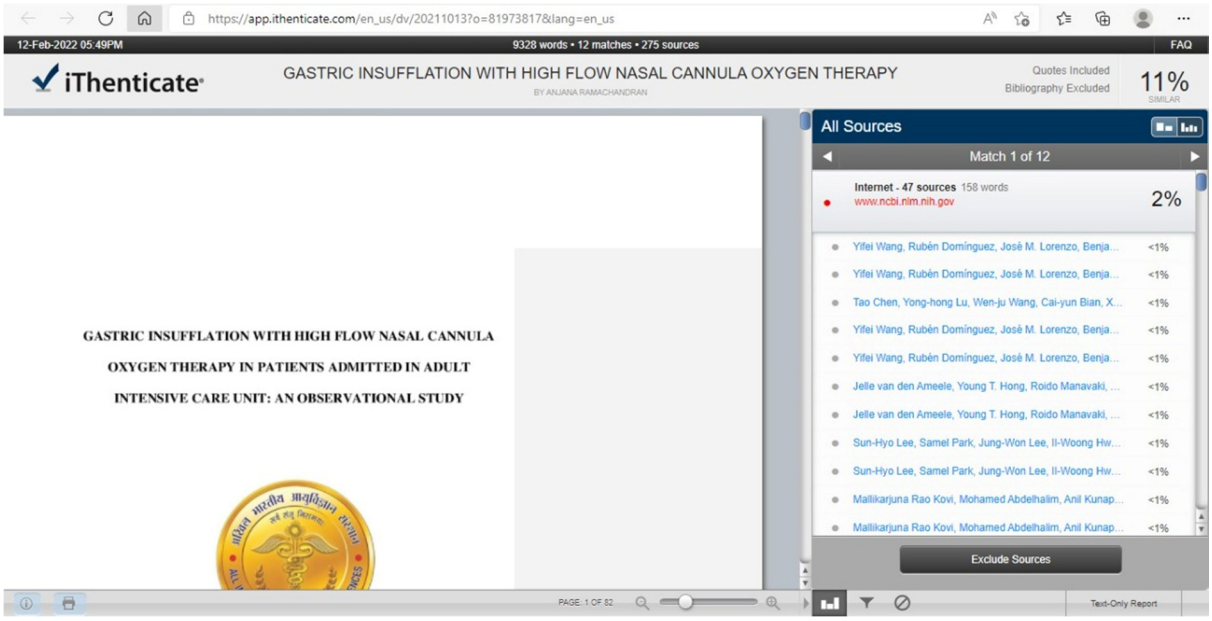
LIST OF FIGURES

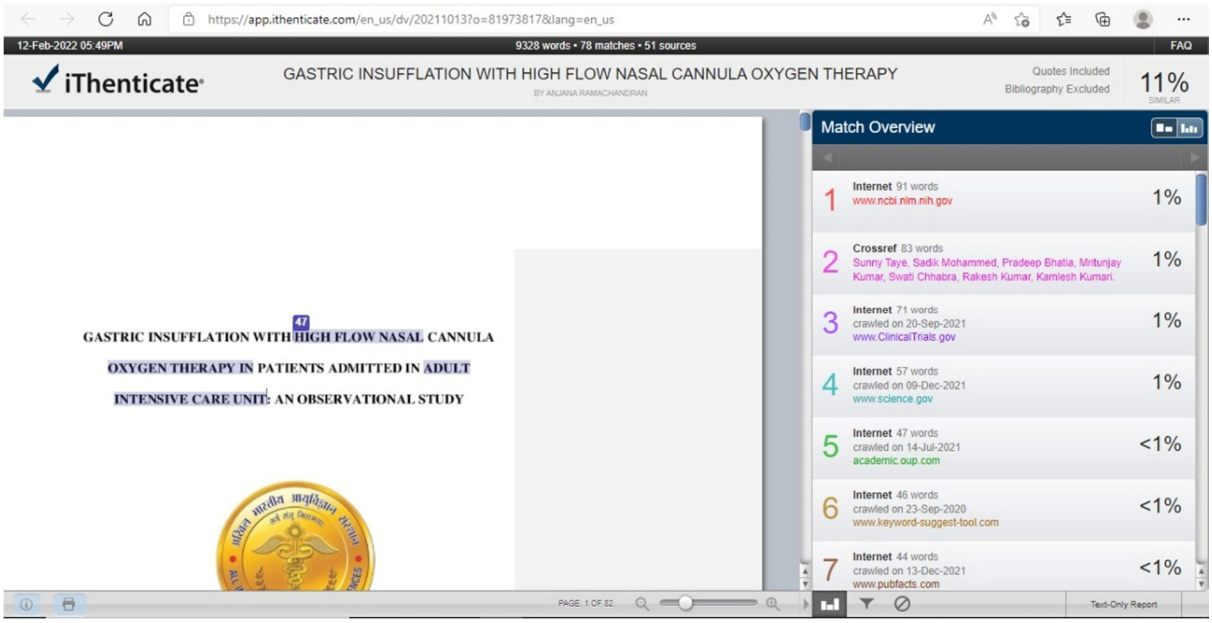
LIST OF TABLES

LIST OF ANNEXURES

PLAGIARISM CHECK CERTIFICATE

Plagiarism check was done on iThenticate Professional Check Software. All the sections except references and review of literature were checked for plagiarism.





SUMMARY

Background: High Flow Nasal Cannula (HFNC) is an increasingly used therapy in the intensive care and emergency medicine settings that allows high flows and fractions of inspired oxygen (FiO_2) at a more physiological level of temperature and humidity. Studies with Non-Invasive Ventilation (NIV) have found that the ventilation volume distributes between lungs and stomach depending on respiratory system resistance and lower esophageal sphincter pressure leading to gastric distension. With the provision of small continuous CPAP effect, HFNC also carries theoretical risk of gastric distension. Our hypothesis was that the use of HFNC in adult patients admitted in ICU would produce air leak in gastric antrum leading to gastric distention.

Methods: We conducted a prospective observational study in a time-span of 1 year to detect gastric insufflation with the help of ultrasonography in patients admitted in the adult intensive care unit at AIIMS Jodhpur receiving oxygen therapy using HFNC. A convenient sampling strategy was used and once the patient was enrolled for study, his/her basal gastric volume and the average number of peristaltic contractions of the stomach in one minute was measured using ultrasonography. Following this, HFNC therapy was started and once the patient was stabilised by the treating intensivist, the flow and FiO_2 set were recorded. The ABG values which include PaO_2, $PaCO_2$, PaO_2/FiO_2, SaO_2 at this FiO_2 were recorded. A 2^{nd}, 3^{rd} and 4^{th} ultrasound scan was done respectively at 10, 20 and 30 minutes after the start of HFNC therapy for looking for air leaks into the stomach and any change in gastric volume. At 10 mins, the average number of peristaltic contractions of the stomach were observed and recorded over one minute. The new vitals and ABG values were recorded after 30 min of start of HFNC therapy. The comfort of the patients on HFNC therapy, the total duration of HFNC application and its outcome were also recorded.

Results

The Antero-Posterior Diameter (APD) at 20 and 30 min were significantly larger (p-value 0.045 and 0.003 respectively) compared to APD at 0 min while there was no significant difference (p-value = 0.67) between APD at 0 min and 10 min. The Transverse Diameter (TVD), Antral Cross-sectional Area (ACSA), Gastric Volume (GV) at 10, 20 and 30 min were significantly larger (p-value <0.0001, <0.0001 and <0.0001 respectively) compared to their measurements obtained at 0 min. The percentage of patients with gastric volume more than 0.8 ml/kg, considered as “at risk stomach” increased from 21% at 0 min to 59% at 30 min after application of HFNC.

There was a significant positive correlation (r=0.541) (p=<0.0001) between HFNC flow and increase in gastric volume. Significantly higher numbers of patients had air leak at 10 min (p-value=0.001), 20 min (p-value<0.0001) and at 30 min (p-value<0.0001) compared with air leak at 0 min. There was a significant increase in the number of peristaltic contractions at 10 mins after initiation of HFNC which supported the above findings. There was a significant increase in the SpO_2 (p value-<0.0001) and a significant decrease in the RR (p value<0.0001) from baseline (0 min) was observed at 30 mins after initiation of HFNC. Keeping FiO_2 constant throughout the study, there was a significant increase in the PaO_2 (p value<0.0001), PF-ratio (p value<0.0001), SaO_2 (p value<0.0001) and a significant decrease in the $PaCO_2$ (p value<0.0001) from the baseline (0min) at 30 mins after application of HFNC. The comfort levels of 35 patients (46.1%) of the study population was good while 34 patients (44.7%) had a fair level of comfort and only 7 patients (9.2%) were uncomfortable with HFNC therapy.

Conclusion

The use of HFNC in adult patients admitted in our intensive care unit is associated with gastric insufflation, which is detectable by ultrasound. The increase in flow of HFNC produces more gastric distention.


INTRODUCTION

Oxygen is a commonly used drug to achieve a normal or near normal oxygen saturation in acutely and chronically ill patients suffering from hypoxaemia. The target saturation for most acutely ill patients must be set 94-98%. A patient specific target range or 88-92% must be set for those at risk of hypercapnic respiratory failure.

Typically, oxygen is delivered either via low flow systems (eg. nasal cannulae or masks) or via high flow systems (eg. Venturi masks, non-rebreathers). These conventional oxygen delivery systems do not warm or humidify the inspired gas and do not deliver a reliable fraction of inspired oxygen leading to poor tolerance when used for prolonged periods. The difference between patient inspiratory flow and delivered flow is large in these systems. High Flow Nasal Cannula (HFNC) is an increasingly used therapy that allows high flows and fractions of inspired oxygen (FiO_2) at a more physiological level of temperature and humidity. Nowadays, it is increasingly used in the intensive care and emergency medicine settings to manage patients with acute hypoxemic respiratory failure as well as to optimize preoxygenation prior to intubation in patients with mild-to-moderate hypoxemia.

The mechanisms by which HFNC acts include small pliable nasal prongs which increases comfort of patient, warming and humidification of secretions which facilitates expectoration, washout of nasopharyngeal dead space that improves efficiency of ventilation, high flow rates that helps in reliable delivery of FiO_2 and a small continuous positive airway pressure (CPAP) effect. Only two parameters need to be set and they are (a) the flow rate and (b) the FiO_2. HFNC is being increasingly used these days in patients with both acute and chronic respiratory failure as a useful alternative to conventional oxygen therapy (COT) and other non-invasive systems of respiratory support. (1, 2) Its other common uses include- as a provision for intubation and extubation support, to treat and support postoperative respiratory failure, to oxygenate tracheostomized patients who are weaning and to oxygenate hypoxemic patients undergoing fiberoptic bronchoscopy. (3, 4)

Studies with Non-Invasive Ventilation (NIV) have found that the ventilation volume distributes between lungs and stomach depending on respiratory system resistance and lower esophageal sphincter pressure leading to gastric distension. (5) With the provision of small continuous CPAP effect HFNC also carries theoretical risk of gastric distension. However, a study done in healthy volunteers proved that the use of HFNC was not associated with increased volume of gastric secretion during spontaneous ventilation. (6) These results can't be extrapolated to critically ill patients. A case report published in 2018 by Satoki Inoue et al,

on a 21month old baby with history of chronic lung disease showed critical abdominal distension with abdominal compartment syndrome after application of HFNC at a flow rate of 20L/min with FiO_2 of 0.35. (7) Therefore, studies are required to evaluate the effect of HFNC therapy on gastric distension.

There is increasing interest in the use of ultrasound to assess and guide the management of critically ill patients. It is a readily available, non invasive, quick and reproducible point of care equipment. Recently its use has been extended to evaluate the gastric antrum and several studies have demonstrated gastric antrum measurement with the help of ultrasonography (8, 9, 10).

We planned an observational study to ultrasonographically evaluate gastric distension in critically ill patients receiving HFNC therapy. We hypothesise that use of HFNC in adult patients admitted in intensive care units could produce air leak in gastric antrum leading to gastric distention.

AIM & OBJECTIVES

AIM:

The aim of this observational study was to detect gastric distension with the help of ultrasonography in patients admitted to the adult intensive care unit and receiving oxygen therapy using HFNC.

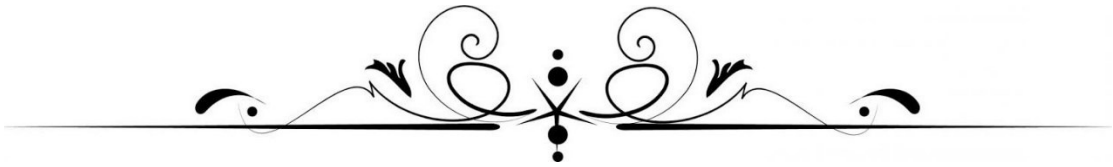
OBJECTIVES:

Primary Objective

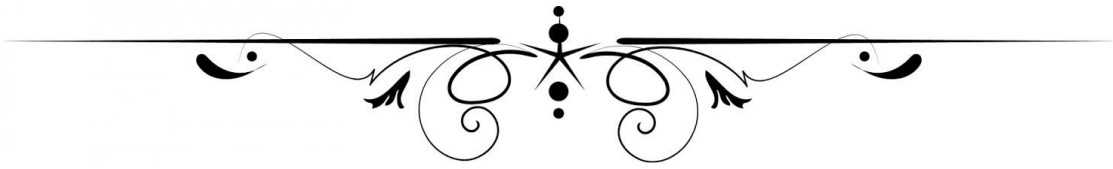
To compare gastric volume at baseline (before HFNC application) with gastric volume at predefined time intervals (10 min, 20 min and 30 min) after application of HFNC using ultrasound.

Secondary Objectives

1. To compare anteroposterior diameter (APD), transverse diameter (TVD) and cross-sectional area (ACSA) of gastric antrum at baseline (before HFNC application) with APD, TVD and ACSA of gastric antrum respectively at predefined time intervals (10 min, 20 min and 30 min) after application of HFNC using ultrasound.
2. To look for and find the incidence of "air leak" defined by qualitative ultrasound as a distended antrum with air content that blurs the posterior gastric wall at predefined time intervals (10 min, 20 min and 30 min) after application of HFNC and compare with baseline using ultrasound.
3. To compare peristaltic contraction of gastric antrum at baseline with peristaltic contraction at 10 min, as a surrogate marker for gastric insufflation.
4. To find the correlation between flow rates and gastric distension.
5. To observe the effect of HFNC on Vitals (heart rate, blood pressure, respiratory rate, SpO_2), ABG parameters ($PaCO_2$, PaO_2, PaO_2/FiO_2, SaO_2), patient comfort and therapy outcome.



REVIEW OF LITERATURE



High flow nasal cannula in Hypoxemic ARF patients

HFNC is an innovative technique that overcomes the patient's spontaneous inspiratory flow and gives heated humidification with effects like pharyngeal dead-space washout, decrease in airway resistance, positive end-expiratory pressure and no dilution of FiO_2. It consists of a flow generator which produces gas flow up to 60 L/min, an air-oxygen blender which can provide FiO_2 up to 100, a humidifier and a nasal cannula.

Indications for using HFNC include different types of ARF (post-operative, post-extubation, palliative care) and in invasive technical procedures like bronchial fibroscopy.

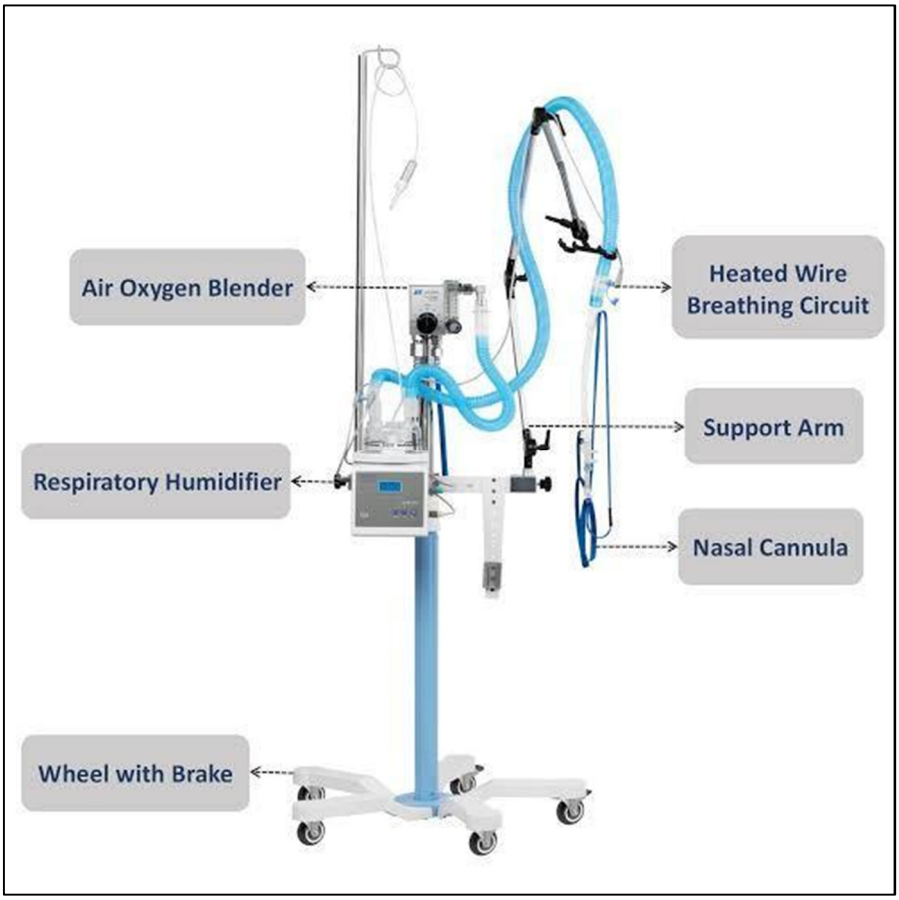


Figure 1: Basic components of HFNC

Sztrymf B et al (2011) conducted a pilot prospective monocentric study to evaluate safety and outcome of HFNC in ICU patients with Acute Respiratory Failure. 38 patients were included and it was found that HFNC significantly reduced RR, HR, dyspnoeic score, supraclavicular retraction and thoracoabdominal asynchrony and increased pulse oximetry as early as 15 minutes after beginning of HFNC. PaO_2 and PaO_2/FiO_2 increased significantly after 1 hour of HFNC in comparison with baseline. (11)

Parke R et al (2011) conducted a prospective Randomised Control Trial to assess effectiveness of nasal HFNC in ICU patients. 60 patients with mild to moderate respiratory failure were randomised to receive nasal high flow (NHF) oxygen therapy or standard high flow face mask (HFFM). On analysis of success of allocated therapy, significantly more NHF patients succeeded their allocated therapy(p=.006). The rate of NIV in the NHF group was 10% compared with 30 % of the HFFM group(p=.10). NHF patients also had significantly fewer desaturation. (p=.009). They concluded that NHF oxygen therapy may be more effective than HFFM in treating mild to moderate hypoxemic respiratory failure. (12)

Domenico Luca Grieco et al (2019) conducted a randomized cross-over trial to do a physiological comparison of HFNC and helmet NIV in hypoxemic patients. 15 hypoxemic patients with PaO_2/FiO_2<200 mmHg received helmet NIV (PEEP≥10cm H_2O, pressure support= 10-15 cm H_2O) and HFNC (50L/min) and their arterial blood gases, dyspnoea and comfort were recorded. Inspiratory effort was estimated by esophageal pressure (PES) swings. PES simplified pressure-time product and transpulmonary pressure swings were measured. As compared to HFNC, helmet NIV increased PaO_2/FiO_2, lowered inspiratory effort, reduced respiratory rate, PES simplified pressure time product and dyspnoea without affecting $PaCO_2$ and comfort. Patients exhibiting lower inspiratory effort on HFNC experienced increases in transpulmonary pressure swings with helmet NIV and was further associated with subsequent need for intubation. They concluded that helmet NIV improves oxygenation, reduces dyspnoea, inspiratory effort and simplified pressure time product, with similar transpulmonary pressure swings, $PaCO_2$ and comfort. (13)

Andrea Vianello et al (2020) conducted an observational study to assess the outcome and safety of O_2 -therapy by high-flow nasal cannula (HFNC) in 28 consecutive patients with severe hypoxemic acute respiratory failure consequent to SARS-CoV-2 infection, unresponsive to conventional O_2 -therapy. 19 patients had a positive response. 9 patients required escalation of treatment to non-invasive ventilation (5 subsequently intubated). Severity of hypoxemia and C reactive protein level were correlated with HFNC failure. None of the staff had a positive swab testing during the study period and the following 14 days. They concluded that HFNC is a safe treatment for less severe patients with SARS-CoV-2 hypoxemic acute respiratory failure. (14)

Other Uses of HFNC

HFNC is accepted as a means to provide oxygen to patients undergoing intubation, both before (preoxygenation) and during the procedure (to prevent desaturation)

Samir Jaber et al conducted a randomised, controlled trial in patients admitted to ICU between July 2015 and February 2016. Hypoxemic patients requiring orotracheal intubation for respiratory failure were randomised to receive preoxygenation using HFNC (flow = 60 L/min, (FiO_2) = 100 %) combined with NIV (pressure support = 10 cmH_2O, PEEP= 5 cmH_2O, FiO_2 = 100 %) in the intervention group (25 patients) or NIV alone in the reference group (24 patients) prior to intubation. The primary outcome was the lowest oxygen saturation (SpO_2) during the intubation procedure. Secondary outcomes were intubation-related complications and ICU mortality. No patient in the intervention group and five patients in the reference group had SPO_2 below 80 percent. There was no significant difference between the groups in intubation-related complications or ICU mortality. Thus, they concluded that adding HFNC for apnoeic oxygenation to NIV prior to orotracheal intubation, may be more effective in reducing the severity of oxygen desaturation than the reference method using NIV alone. (15)

Recent studies show that HFNC can also be used in patients with hypercapnic respiratory failure, especially if they are non-compliant to NIV treatment

Rosa Di Mussi et al (2018) conducted a cross over study on 14moderate to severe COPD patients admitted in ICU between December 2015 and December 2016 and required mechanical ventilation for acute hypercapnic respiratory failure. Patients ready for extubation, as assessed by treating clinician, were eligible for the study. After extubation, each patient received two 1 hr periods of HFNC (HFNC1 and HFNC2) alternating with 1 hr of conventional low flow oxygen therapy via face mask. The FiO_2 was titrated to achieve arterial oxygen saturation of 88-92%. The electric activity of diaphragm (EAdi) was studied. It increased from a mean of 15.4 to 23.6 microVolt switching from HFNC1 to conventional O_2 and then returned to 15.2 switching back to HFNC2. They concluded that HFNC as compared with conventional oxygen therapy, significantly decreases neuro ventilatory drive and work of breathing in COPD patients recovering from acute respiratory failure after a planned extubation. (16)

Aerophagia, nausea, vomiting and aspiration

The stomach may insufflate with inspiratory gas during non-invasive ventilation if the pressures exceed 20-25cm H_2O at lower esophageal sphincter. Due to multiple factors that increase airway pressures like cough, dyssynchronous ventilation aerophagia can happen even at lower set pressures.

Lionel Bouvet et al (2014) conducted a prospective, randomized, double blind study in which 67 patients were allotted to 4 groups based on pressure applied during controlled pressure ventilation: 10,15,20,25 cm H_2O. Propofol and remifentanil was given for anaesthesia and no neuromuscular blockade was done. Once eyelash reflex was lost, face mask ventilation started for 2 mins. Patient was then auscultated. The cross-sectional antral area was measured before and after facemask ventilation and thus the gastric insufflation was studied. Results showed statistically significant increase in incidences of gastric insufflation with inspiratory pressure from 0% in group P10 to 41% in group P25 according to auscultation and from 19 to 59% according to USG. Statistically significant increase in antral area was obtained in group P20 and P25 with insufficient lung ventilation in P10. Thus, they concluded that inspiratory pressure of 15 was best as it showed proper lung ventilation with reduced occurrence of gastric insufflation. (8)

No study till date has proven gastric insufflation with HFNC but an increase in mean nasopharyngeal pressures with increase in flow has been noticed.

Elizabeth McLellan et al (2020) conducted a prospective, interventional assessor-blinded study in 60 subjects to evaluate effect of HFNC on gastric content and gastric distension in healthy fasted adult volunteers assessed by ultrasonography. 60 subjects were enrolled. Primary outcome was the volume of gastric secretions and the secondary outcome was the incidence of gastric insufflation and distribution of gastric antral grades. They concluded that there was no evidence that treatment with HFNC at flow rate up to 70 L/min for 30 min resulted in gastric distension or an increase in gastric secretions in healthy volunteers breathing spontaneously. (6)

Sud et al conducted a blinded, non-randomised retrospective study to compare the gastric volumes acquired immediately after intubation measured by computed tomography in two series of adult patients undergoing percutaneous thermal ablation of liver cancer under general anaesthesia: 50 received peri-intubation high flow nasal oxygen therapy and another

50 received conventional facemask pre-oxygenation and ventilation before intubation. Median gastric volume was 24 cm^3 in the high flow nasal oxygen therapy group and 23.8cm^3 in the facemask group. There was no difference in the volume of gastric gas measured by computed tomography imaging between the two groups. They concluded that a small volume of gas is commonly present after induction of anaesthesia, but that the use of peri intubation high flow nasal oxygen therapy for preoxygenation and during apnoea does not increase this volume compared with conventional facemask pre-oxygenation and ventilation. (9)

Parke RL et al (2011) conducted a prospective descriptive study in patients who were scheduled for elective cardiac surgery in a tertiary care cardiothoracic and vascular ICU to determine the relationship between flow and pressure with the Optiflow nasal high flow oxygen therapy system. Measurements were performed with nasal flow oxygen at flows of 30, 40 and 50 L/min with patients' mouths both open and closed. They concluded that mean nasopharyngeal pressure during nasal high flow oxygen increases as flow increases. (17)

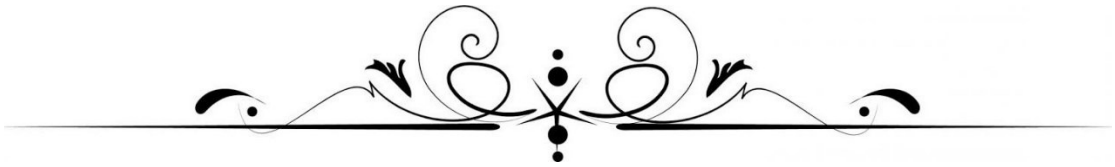
A case report showing the need to consider HFNC as a positive pressure ventilation system and that critical overdistension can occur by use of HFNC was published in 2018.

Satoki Inoue et al (2018) published a case report on a 21month old boy with a history of chronic lung disease who was admitted in ICU. He had a history of upper respiratory infection and fever for a couple of days. He gradually developed hypoxia (SPO_2<90%) with oxygen administration. His airway was immediately secured with a tracheal tube and mechanical ventilation was started. After 5 days he was extubated and HFNC therapy was started at 20L/min with an FiO_2 of 0.35. As the child developed severe stridor, a nasal airway was placed in the left nostril. Following this, the child showed signs of distress and critical abdominal distension was noted. A subsequent chest x-ray revealed the deep placement of nasal airway and gastric insufflation due to this. The child also showed features of abdominal compartment syndrome. Immediately, the nasal airway was removed and HFNC flow reduced to 10 L/min. Frequent suctioning and continuous gastric drainage was done. By this, they concluded that HFNC needs to be recognized as a positive pressure ventilation system and that critical over-distension of the abdomen can occur by HFNC. (18)

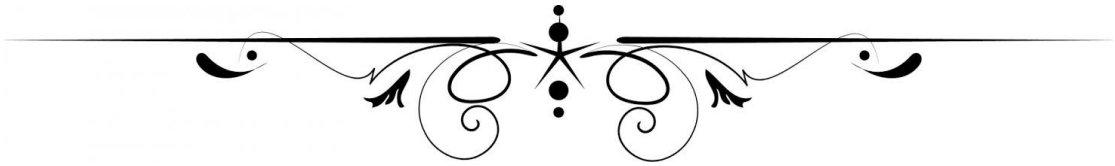
Ultrasonography and gastric antrum

Perlas A et al conducted a prospective observational study to examine the feasibility of using bedside ultrasonography for assessing gastric content and volume. In pilot phase 1, 18 healthy volunteers were examined to assess gastric antrum, body and fundus in cross-section in 5 prandial states. In phase 2, authors concentrated on ultrasonographic examination of gastric antrum to see for correlation between antral cross-sectional area and gastric volume. Results showed that gastric antrum provided the most reliable quantitative information for gastric volume. Sonographic assessment of the body and antrum of stomach provides qualitative information regarding the gastric content. They concluded that bedside ultrasonography can be a useful medium for determining gastric content and volume. (10)

S R Hamada et al conducted a prospective cross-sectional study in 55 critically ill patients to assess the feasibility and validity of ultrasonographic measurement of gastric antral cross-sectional area to predict gastric volume (usCSA) and the use of computed tomography as a reference to measure gastric volume. usCSA measurements were performed within the hour preceding CT scan. Antral usCSA measurements were feasible in 95% of cases and were positively correlated with gastric volume measured by CT scan when performed in “good” conditions. There was good reproducibility of measurements and there was clinically acceptable agreement between measurements performed by radiologists and intensivists. They concluded that ultrasonographic measurement of the Antral Cross-sectional area is feasible and reliable in the majority of critically ill patients. (19)



MATERIALS & METHODS



STUDY SETTING

The study was conducted in the department of Anaesthesiology and Critical Care, AIIMS, Jodhpur after getting approval from the institutional ethical committee (Certificate Reference Number- AIIMS/IEC/2019-20/995 dated 18/11/2020).

STUDY DESIGN

Prospective observational study

STUDY DURATION

The study was completed in a timespan of one year after getting ethical approval and CTRI registration (CTRI/2021/03/031608) (from January 2021 to December 2021).

STUDY PARTICIPANTS

All patients who were admitted in the adult intensive care unit in whom the need of HFNC therapy was recognised by the treating intensivist.

INCLUSION CRITERIA:

- Adult patients aged above 18 yrs
- Tachypnoeic (RR>20) and in need of oxygen therapy (i.e. SPO_2< 92) as recognised by an intensivist

EXCLUSION CRITERIA:

- Pregnant women
- Patients who were in severe respiratory failure requiring immediate tracheal intubation and mechanical ventilation.
- Patients with SPO_2 >92%
- Obese patients and postoperative patients after upper abdominal surgery, where interpretation with abdominal ultrasound was difficult.
- Patients who were on continuous Nasogastric tube aspiration.
- Patients with serious cardiovascular, renal or hepatic illness.
- Patients with abnormalities of face or who are post-surgery of face, nose or airway that preclude an appropriate fitting nasal cannula
- Psychiatric, agitated or non-cooperative patients

- Patients with altered sensorium

SAMPLING STRATEGY

Simple random probability sampling

SAMPLE SIZE

Sample size calculation was based on the primary outcome measure of our study i.e. increase in gastric volume. The gastric volume considered as 'at risk stomach' has been defined as 0.8 ml/kg. (19) We assumed that 40% patients receiving HFNC would develop 'at risk stomach' compared to 10 % without HFNC. A total of 76 subjects were required for a significance of 5% and power of 80% to detect this difference.

DATA COLLECTION

All patients admitted in the adult intensive care unit in whom the need of HFNC therapy was recognised by the treating intensivist were enrolled in the study. After giving detailed description about the study that is being conducted and obtaining informed consent, a brief history of each patient was taken regarding relevant comorbidities and duration of respiratory illness and medications. Physiological data including vital signs such as heart rate, respiratory rate, blood pressure, pulse oxygen saturation were recorded. Once the decision of HFNC therapy was made by the treating intensivist, the patient's basal gastric volume was measured using ultrasonography. The average number of peristaltic contractions of the stomach in one minute was calculated after counting the peristaltic contractions of the stomach for a time period of 5 minutes.

Following this, HFNC therapy was started and once the patient was stabilised by the treating intensivist, the flow and FiO_2 set were recorded. The ABG values which include PaO_2, $PaCO_2$, PaO_2/FiO_2, SaO_2 at this FiO_2 was recorded. A 2^{nd}, 3^{rd}, 4^{th} ultrasound scan was done respectively at 10, 20 and 30 minutes after the start of HFNC therapy. These scans would look for air leaks into the stomach and any change in gastric volume. At 10 mins, the average number of peristaltic contractions of the stomach in one minute was calculated after counting the peristaltic contractions of the stomach for a time period of 5 minutes. The air leak in the gastric antrum, defined by qualitative ultrasound as a distended antrum with air content that blurs the posterior gastric wall was recorded. The new vitals and ABG values were recorded after 30 min of start of HFNC therapy. It was ensured that only cases with a constant FiO2

and Flow requirement, as set by the intensivist for the study time period of 30 minutes were included in the study. The comfort of the patients on HFNC therapy were recorded at the end of the study on a scale of good, fair or poor based on their subjective feelings and opinions. The total duration of HFNC application and its outcome were also recorded.

Ultrasound assessment of volume

Portable ultrasound device (LOGIQ e; GE medical system; China) with a curvilinear low frequency (3.5-5 MHz) transducer was used for quantitative measurement of the antral cross-sectional area (ACSA). All the ultrasound examinations were performed by the same anaesthesiologist, who was supervised by an experienced radiologist till the anaesthetist was confident to perform the ultrasound assessment independently. To ensure consistent measurements, three scans were performed in each patient at each time of observation. If there was a difference of more than 0.5 cm in craniocaudal and transverse dimension measurements between any two of the images, then the patient's data was excluded from the study. All patients would then undergo quantitative assessment of ACSA, in the right lateral position with 45 degrees of head elevation. The gastric antrum was imaged in the sagittal plane in the epigastrium, along the edge of the left lobe of liver, and at the level of the aorta. The maximal anteroposterior diameter (D1) and transverse diameter (D2) of a single section of the gastric antrum was determined.

$$ACSA = (\pi \times D1 \times D2) \div 4$$

The mean values of three consecutive measurements of D1 and D2 were used to calculate the ACSA. From the ACSA, gastric volume was calculated. The mathematical model reported by Bouvet and colleagues based on gastroscopic fluid assessment with a reference standard of nasogastric suction was used for calculation of gastric volume from ACSA (32)

(ml) = -215+57 log ACSA (mm^2)-0.78 age(year)-0.16 height(cm)-0.25

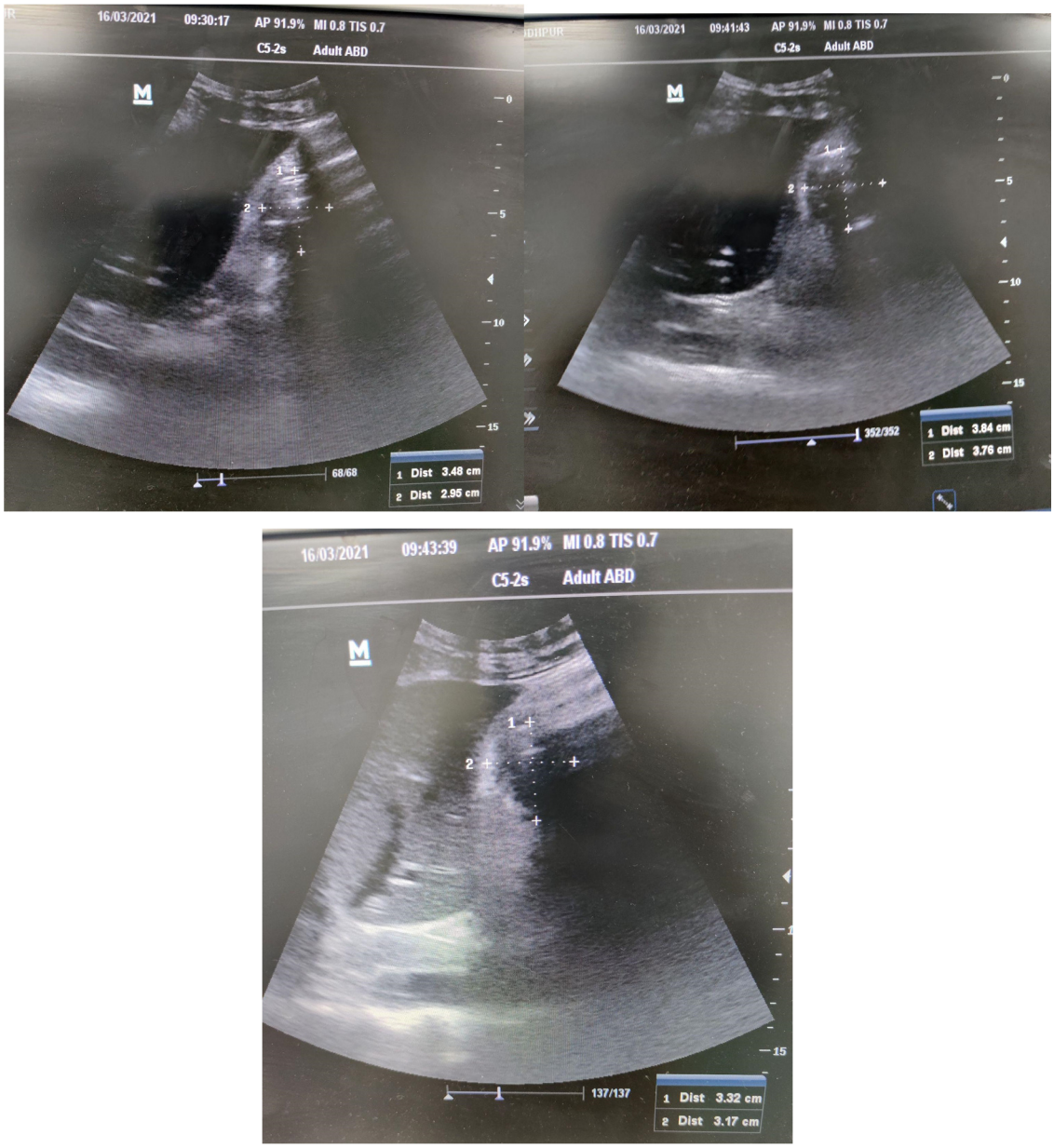
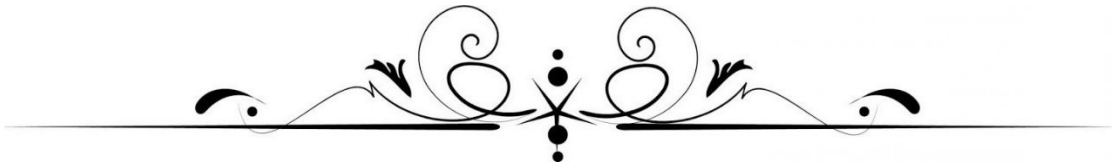


Figure 2: USG images showing anteroposterior diameter (D1) and transverse diameter (D2) of gastric antrum in a patient at different time intervals after application of HFNC

STATISTICAL ANALYSIS

The data collected was entered in Microsoft Excel and checked for any inconsistency. All statistical analyses were carried out by using SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Nominal variables were described using counts and percentages, and were analysed using Chi square test or Fisher Exact test. Ordinal variables were described using median and interquartile range and were analysed using Mann Whitney U test for unpaired data and Wilcoxon test for paired data. Interval and ratio scales were described using mean and standard deviation, and were analysed using unpaired t-test or paired t-test as applicable. Spearman's correlation was calculated for finding association between HFNC flow rate and gastric distension. P value <0.05 was considered as significant.



OBSERVATIONS & RESULTS

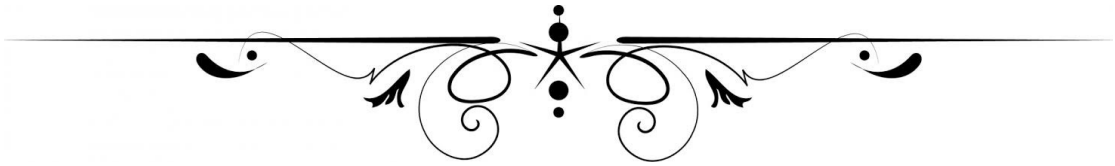


Table 1: Distribution of Age (years) in study population

PARAMETER	RANGE	FREQUENCY	PERCENTAGE
AGE (years)	21-30	5	6.5
	31-40	7	9.2
	41-50	9	11.8
	51-60	16	21
	61-70	27	35.5
	71-80	7	9.2
	81-90	5	6.5
	MEDIAN (IQR) (RANGE)	61.50 (46.5, 68.0) (27-87)	

The median (IQR) (range) age (years) in our study population was 61.5 (46.5, 68) (27 - 87). The maximum number of patients enrolled for the study (35.5%) belonged to the age group 61-70 years and only a minority (6.5%) constituted both the age groups, 21-30 years and 81-90 years.

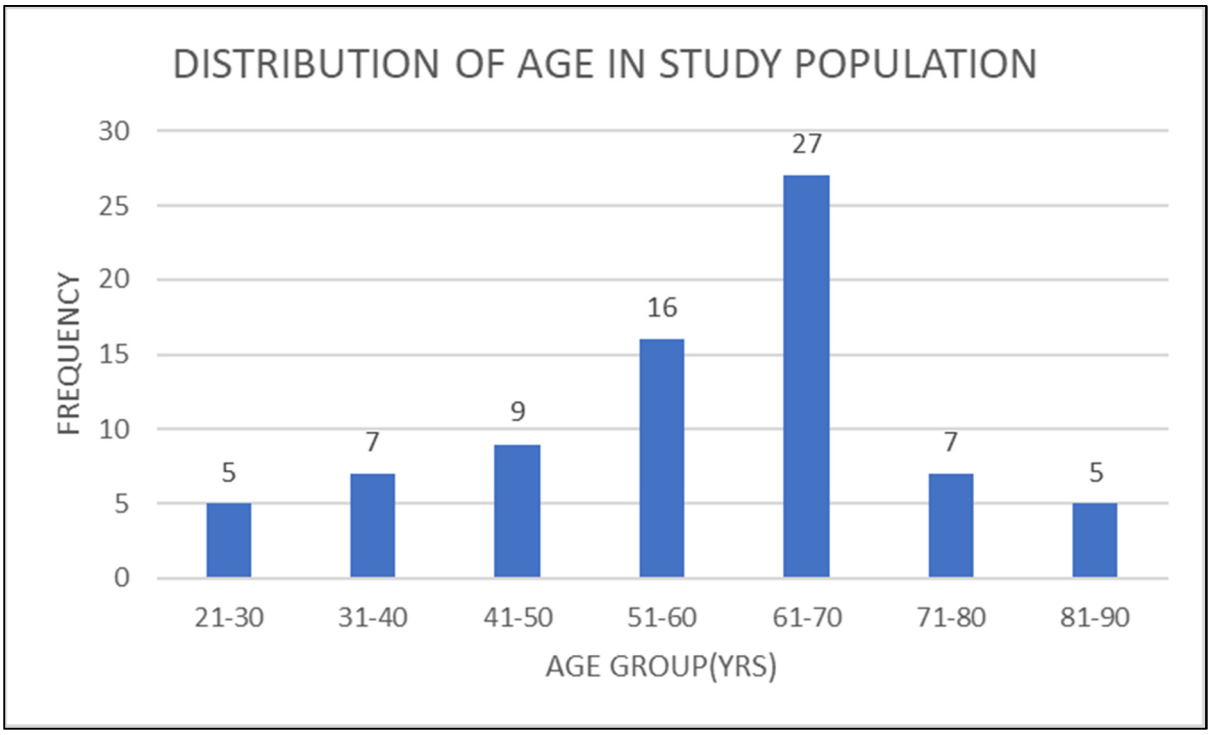


Figure 3: Bar chart showing Distribution of Age(years) in study population

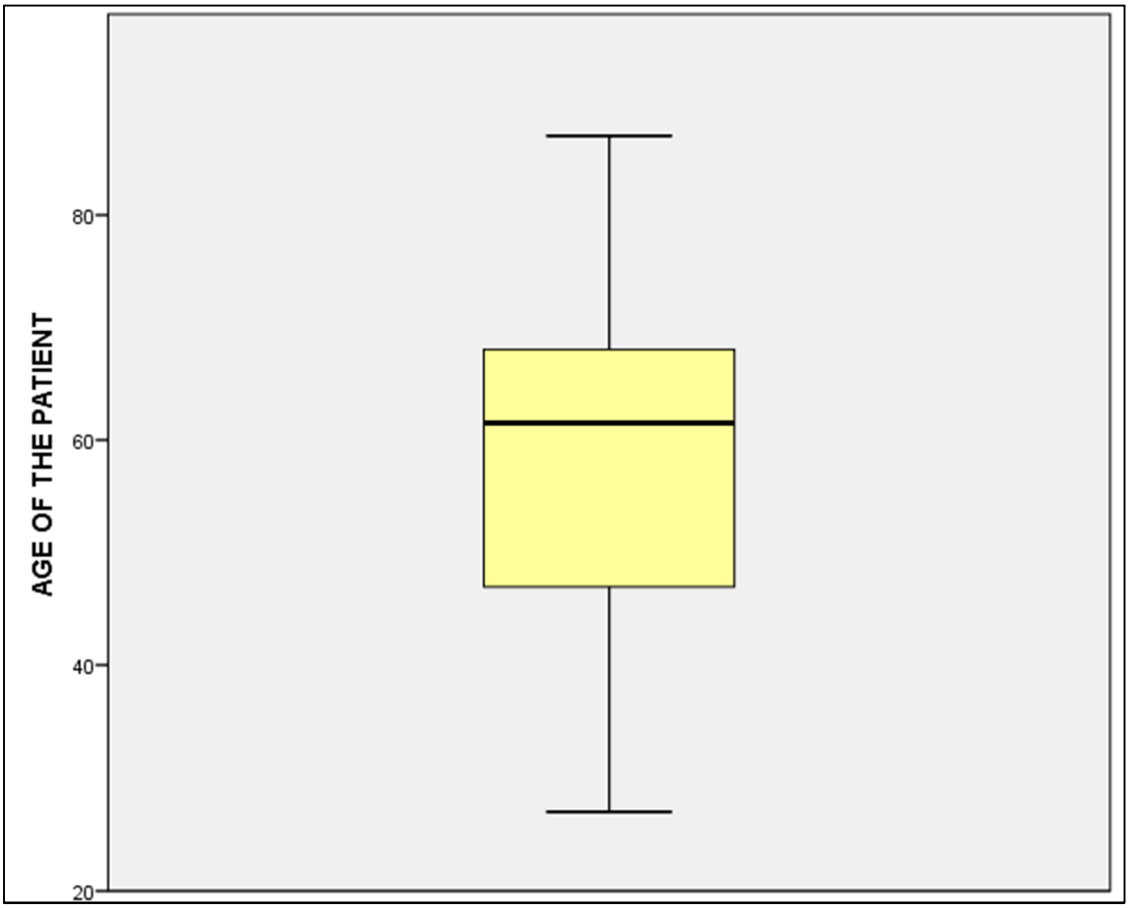


Figure 4: Box plot showing Median (IQR) (range) age (years) in the study population.

Table 2: Distribution of Gender in study population

PARAMETER		FREQUENCY	PERCENTAGE
GENDER	MALE	52	68.4
	FEMALE	24	31.6

In our study population, 68.4% (52) of the patients were male and 31.6% (24) of the patients were female.

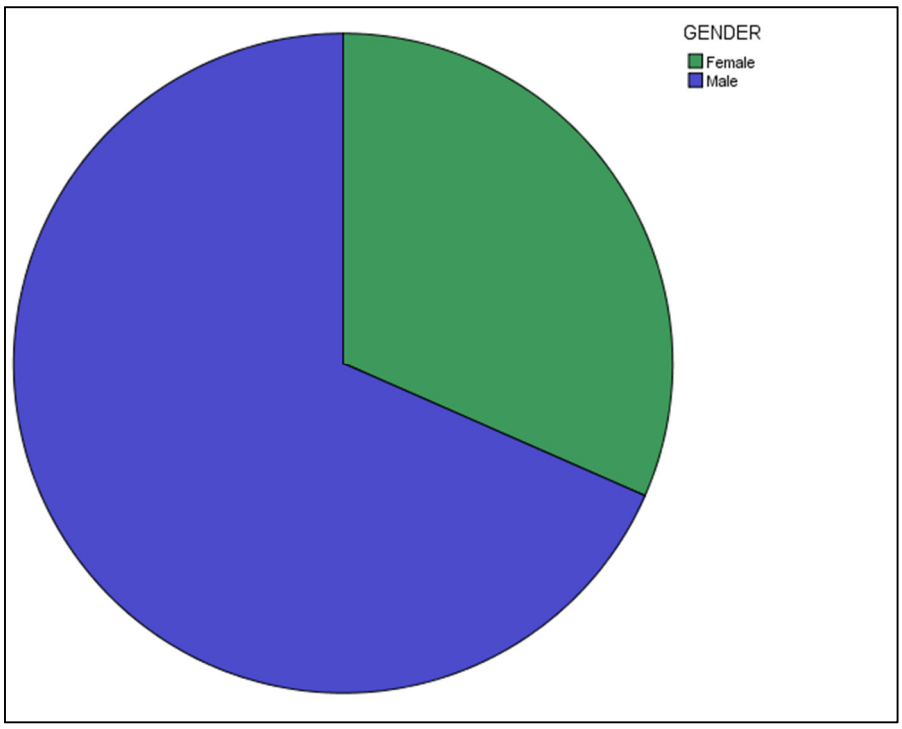


Figure 5: Pie Chart showing Distribution of Gender in study population.

Table 3: Distribution of Height (cm) in study population

PARAMETER	RANGE (in cm)	FREQUENCY	PERCENTAGE
HEIGHT (cm)	141-150	1	1.3
	151-160	24	31.5
	161-170	40	52.6
	171-180	11	14.4
	MEDIAN (IQR) (RANGE)	165 (159, 168) (149-179)	

The median (IQR) (range) height (cm) in our study population was 165(159, 168) (149-179). Maximum number of patients enrolled for the study (52.6%) had height in the range of 161-170 cm and only a minority of (1.3%) had height below 150 cm.

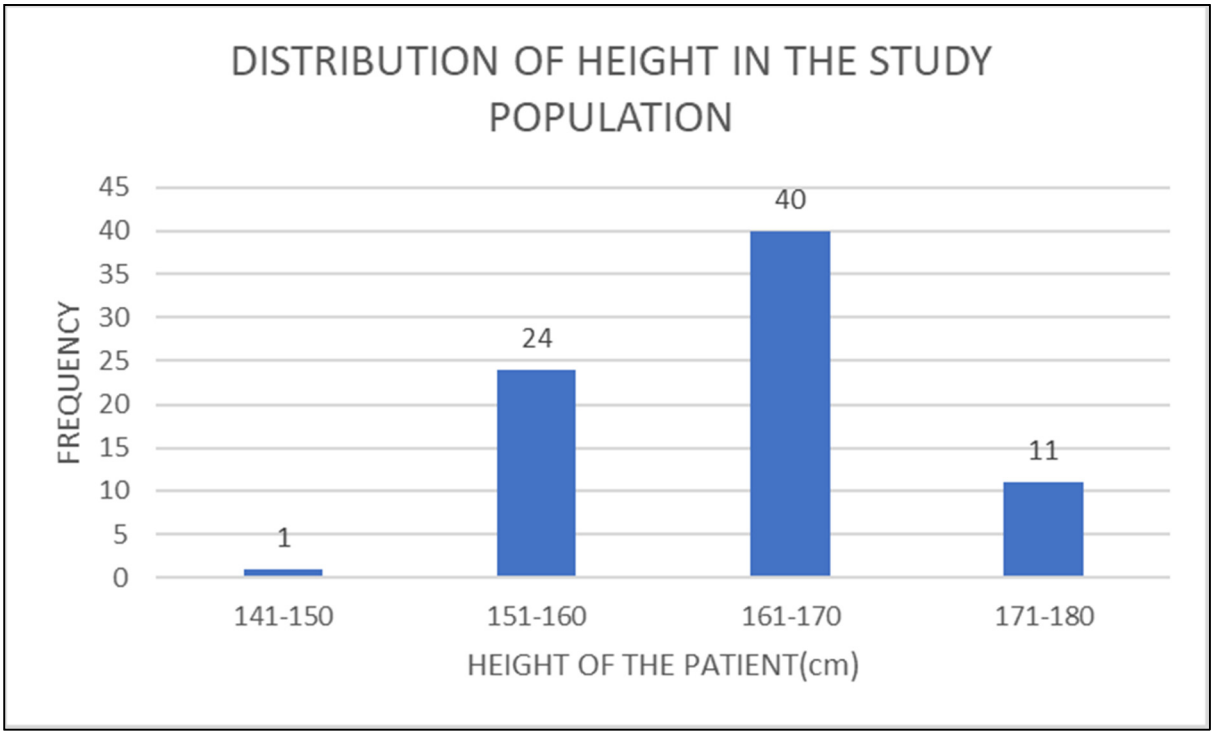


Figure 6: Bar chart showing distribution of Height (cm) in the study population

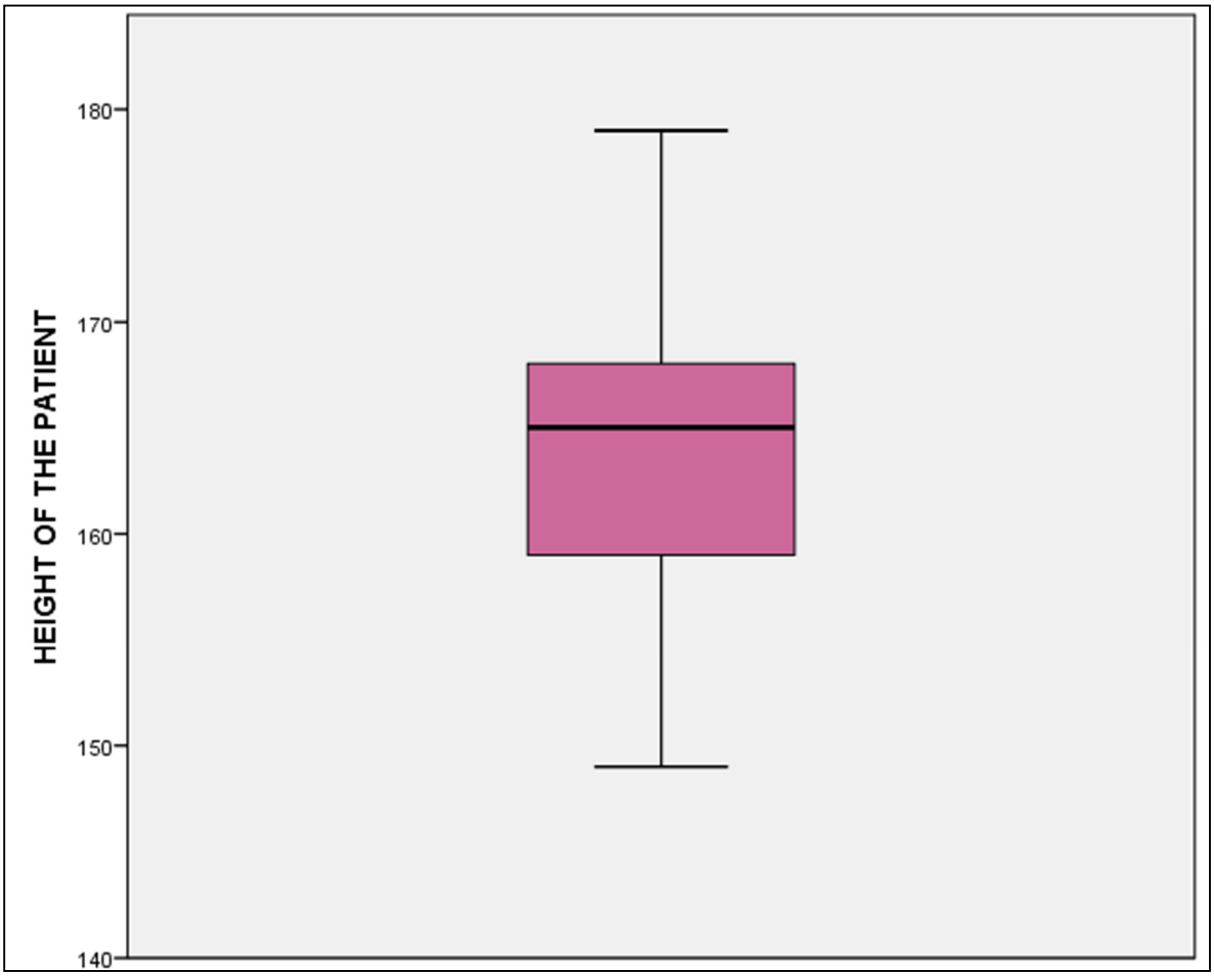


Figure 7: Box plot showing median (IQR) (range) Height (cm) in study population.

Table 4: Distribution of Weight (in kilogram) in study population

PARAMETER	RANGE (kg)	FREQUENCY	PERCENTAGE
WEIGHT (kg)	41-50	2	2.6
	51-60	24	31.5
	61-70	20	26.3
	71-80	25	32.8
	81-90	5	6.5
	MEDIAN (IQR) (RANGE)	68.5 (59, 74) (45-90)	

The median (IQR) (range) weight (kg) in our study population was 68.5 (59, 74) (45-90). Maximum number of patients enrolled for the study (32.8%) had weight in the range of 71 to 80 kg and only a minority of (2.6%) had weight below 50 kg. Only 6.5% of the study population had weight above 80 kg.

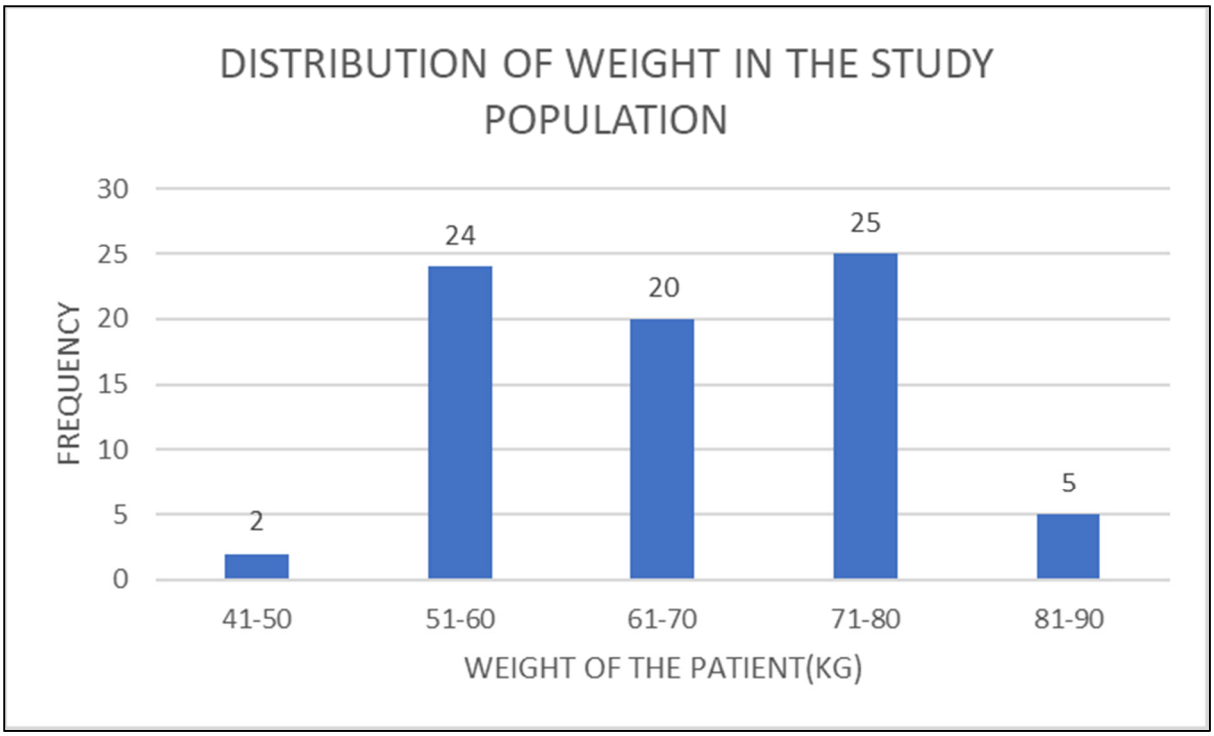


Figure 8: Bar chart showing distribution of weight in the study population

.

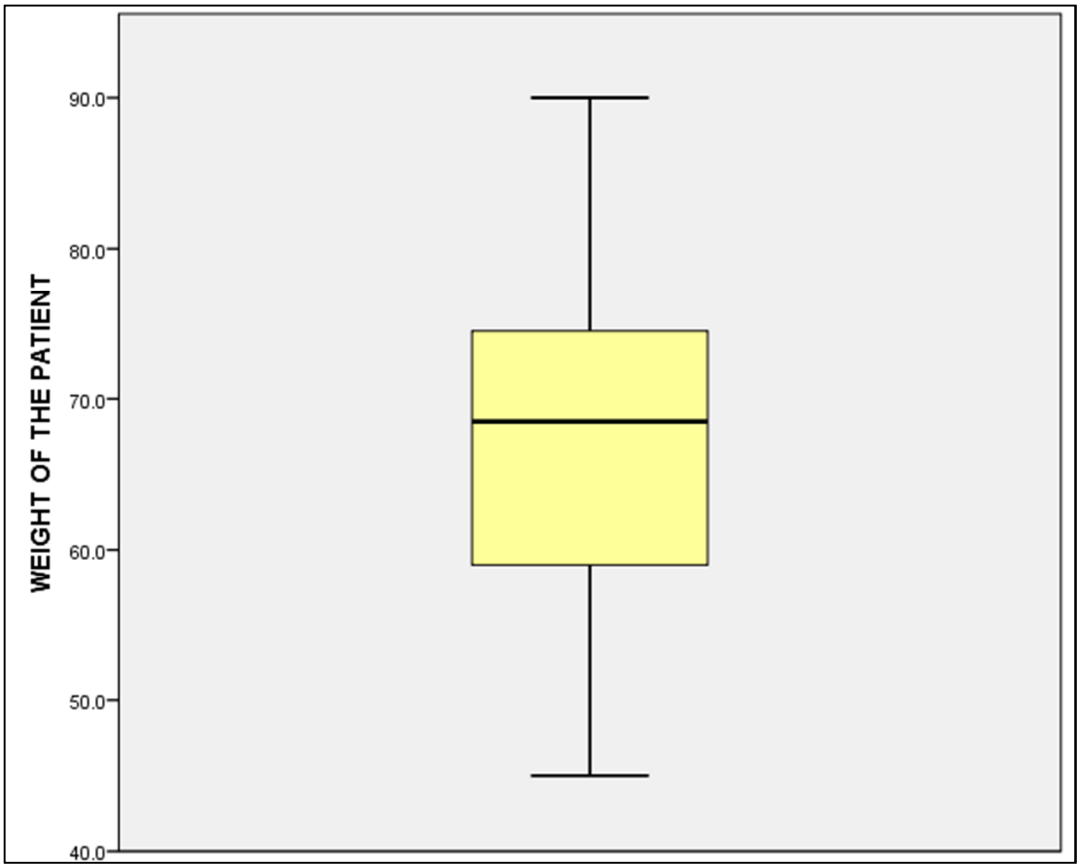


Figure 9: Box Plot showing median (IQR) (range) Weight (kg) in study population.

Table 5: Distribution of Body Mass Index (in kilogram per square meter) in study population

PARAMETER	RANGE (kg/m2)	FREQUENCY	PERCENTAGE
BMI (kg/m^2)	15-20	4	5.2
	21-25	43	56.5
	26-30	27	35.5
	31-35	2	2.6
	MEDIAN (IQR) (RANGE)	25.1 (22.9, 27.2) (16.3-31.2)	

The median (IQR) (range) BMI (kg/m^2) in our study population was 25.1 (22.9, 27.2) (16.3-31.2). Maximum number of patients enrolled for the study (56.5%) had BMI in the range of 21 to 25 kg/m^2. Only 4% of the study population had BMI in between 15-20 kg/m^2 and 2% had BMI in the range of 31-35 kg/m^2.

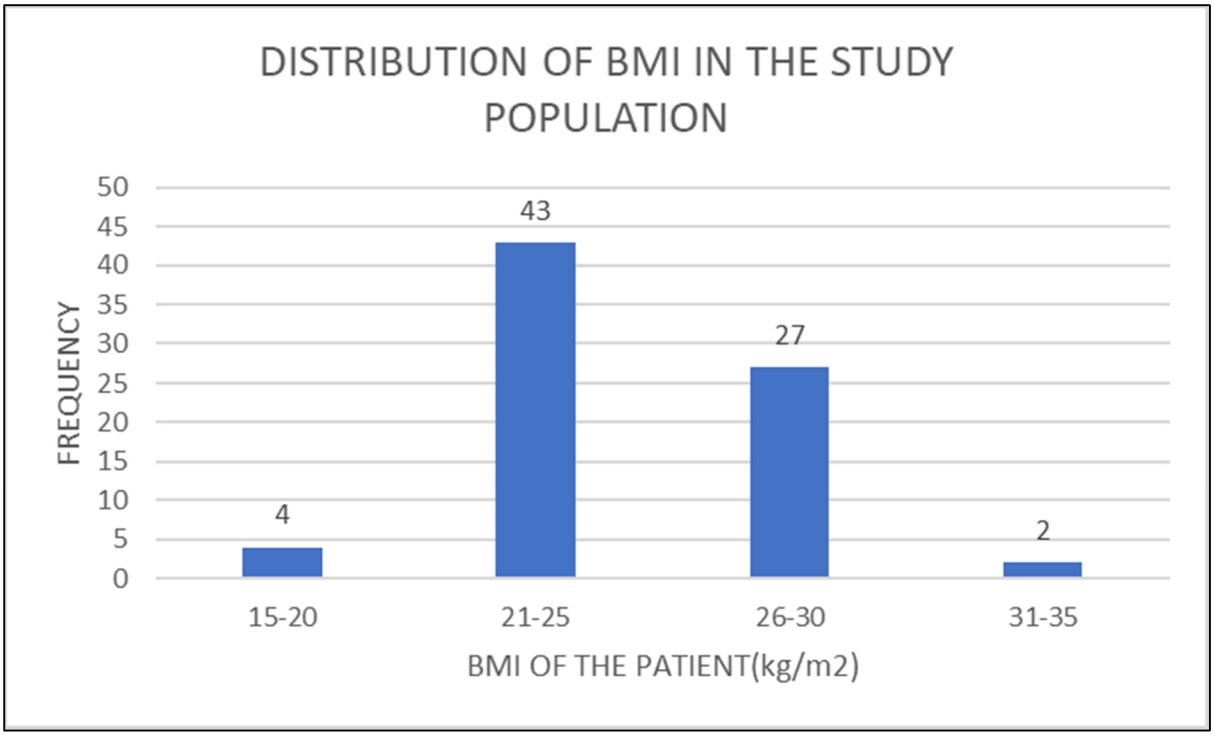


Figure 10: Bar chart showing distribution of BMI(kg/m^2) in study population.

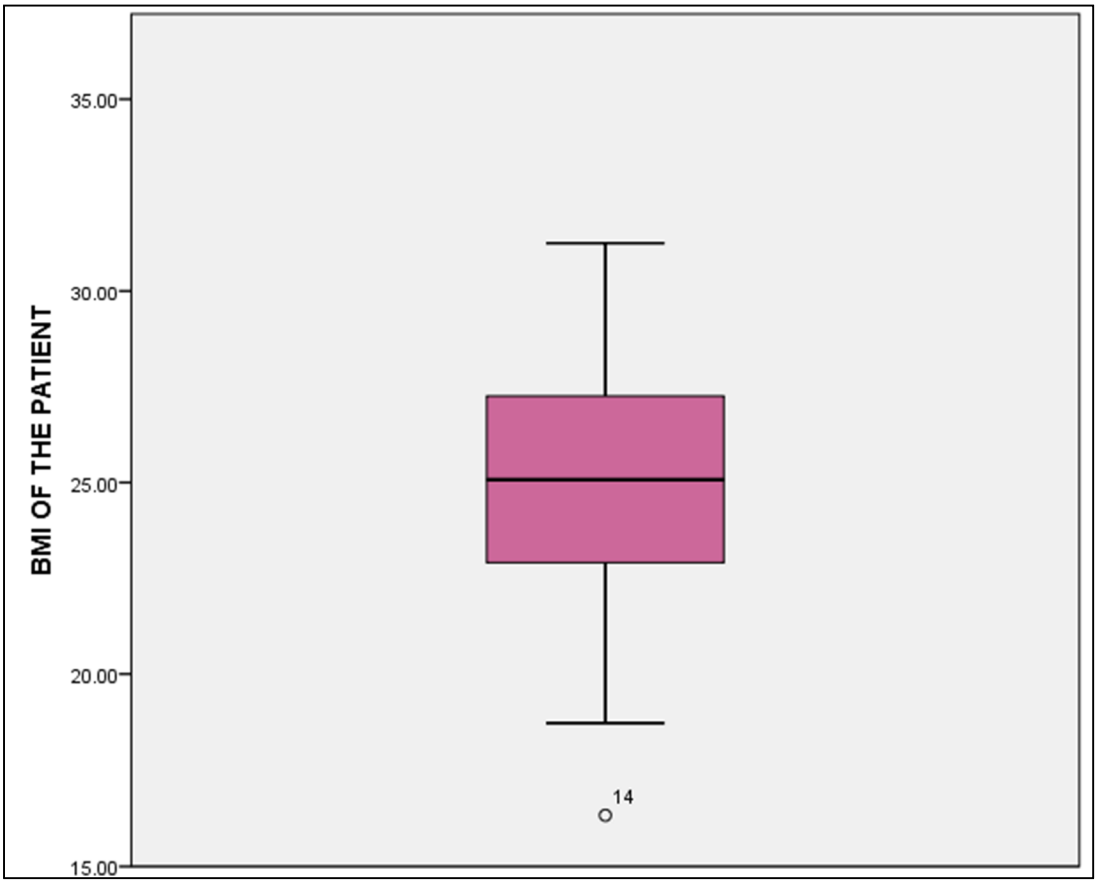


Figure 11: Box Plot showing median (IQR) (range) BMI (kg/m^2) in study population.

Table 6: Distribution of Comorbidities in the study population

PARAMETER		FREQUENCY	PERCENTAGE
COMORBIDITIES	DM	11	14.4
	HTN	7	9.2
	IHD	3	3.9
	CKD	1	1.3
	DM+HTN	9	11.8
	DM+IHD	4	5.2
	DM+CKD	1	1.3
	DM+ASTHMA	1	1.3
	HTN+IHD	2	2.6
	HTN+HYPOTHYROIDISM	1	1.3
	HTN+CKD	1	1.3
	DM+HTN+IHD	2	2.6
	DM+HTN+HYPOTHYROIDISM	1	1.3
	DM+HTN+CKD	1	1.3
	HTN+IHD+CKD	1	1.3
	PARKINSONISM	1	1.3
	NONE	29	38.1

DM: Diabetes Mellitus, HTN: Hypertension, IHD: Ischemic Heart Disease, CKD: Chronic Kidney Disease,

In our study population, 61.9% (47) of the patients were associated with at least one comorbidity. Diabetes mellitus was the most common comorbidity found followed by hypertension. 14.4% and 9.2% of the study population was diabetic only and hypertensive only respectively. 11.8% of the total patients were both diabetic and hypertensive. Other comorbidities associated were Coronary heart disease, Ischemic heart disease, Chronic kidney disease, Hypothyroidism, Asthma and parkinsonism. 3.9% of the study population

had both Diabetes mellitus and Coronary Artery Disease. 29% of the patients had no associated comorbidities.

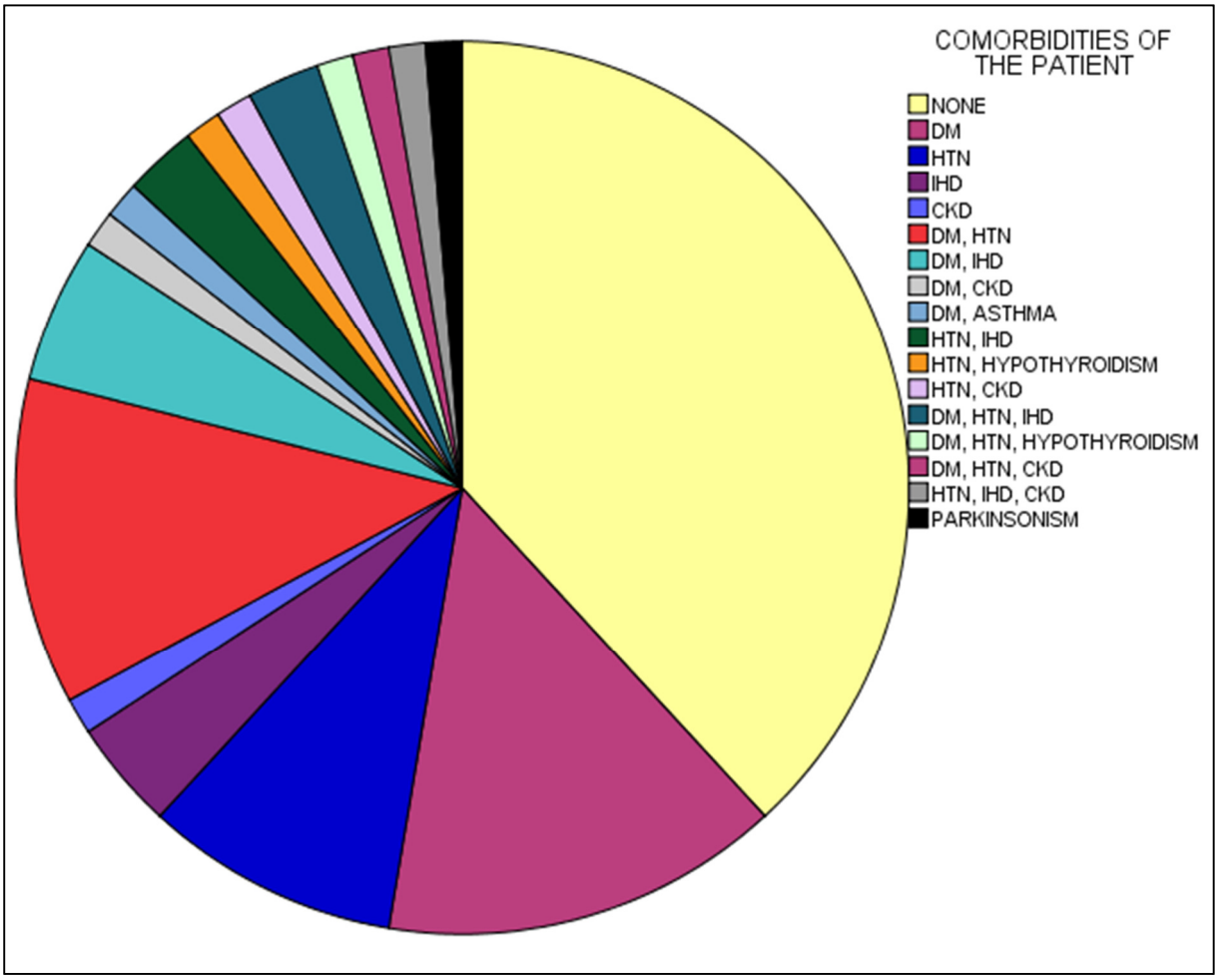


Figure 12: Pie chart showing Distribution of Comorbidities in the study population

Table 7: Distribution of Duration of Illness (in number of days) in the study population

PARAMETER	RANGE	FREQUENCY	PERCENTAGE
DURATION OF ILLNESS (days)	1-10	25	32.8
	11-20	37	48.6
	21-30	13	17.1
	31-90	1	1.3
	MEDIAN (IQR) (RANGE)	14 (7.25, 20) (2-90)	

The median (IQR) (range) duration of illness (days) in our study population was 14 (7.25, 20) (2-90). Maximum number of patients (48.6%) had a duration of illness in the range of 11 to 20 days.

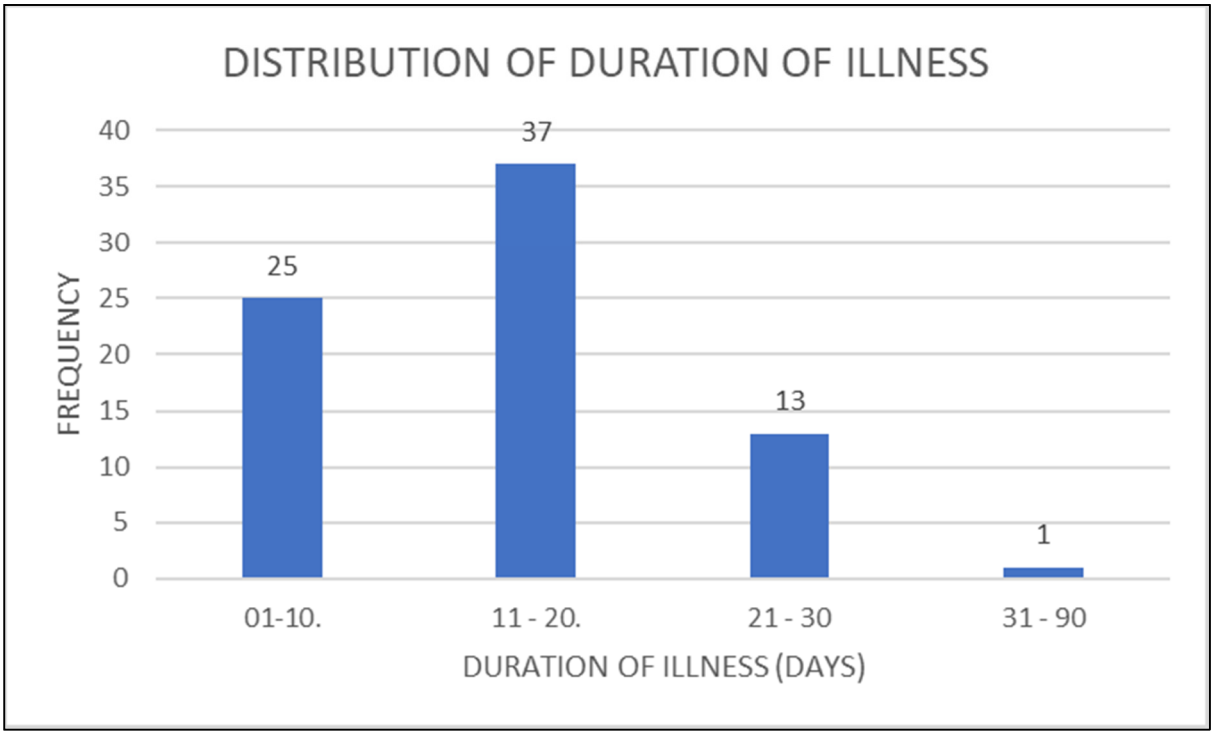


Figure 13: Bar chart showing Distribution of Duration of illness (days) in study population.

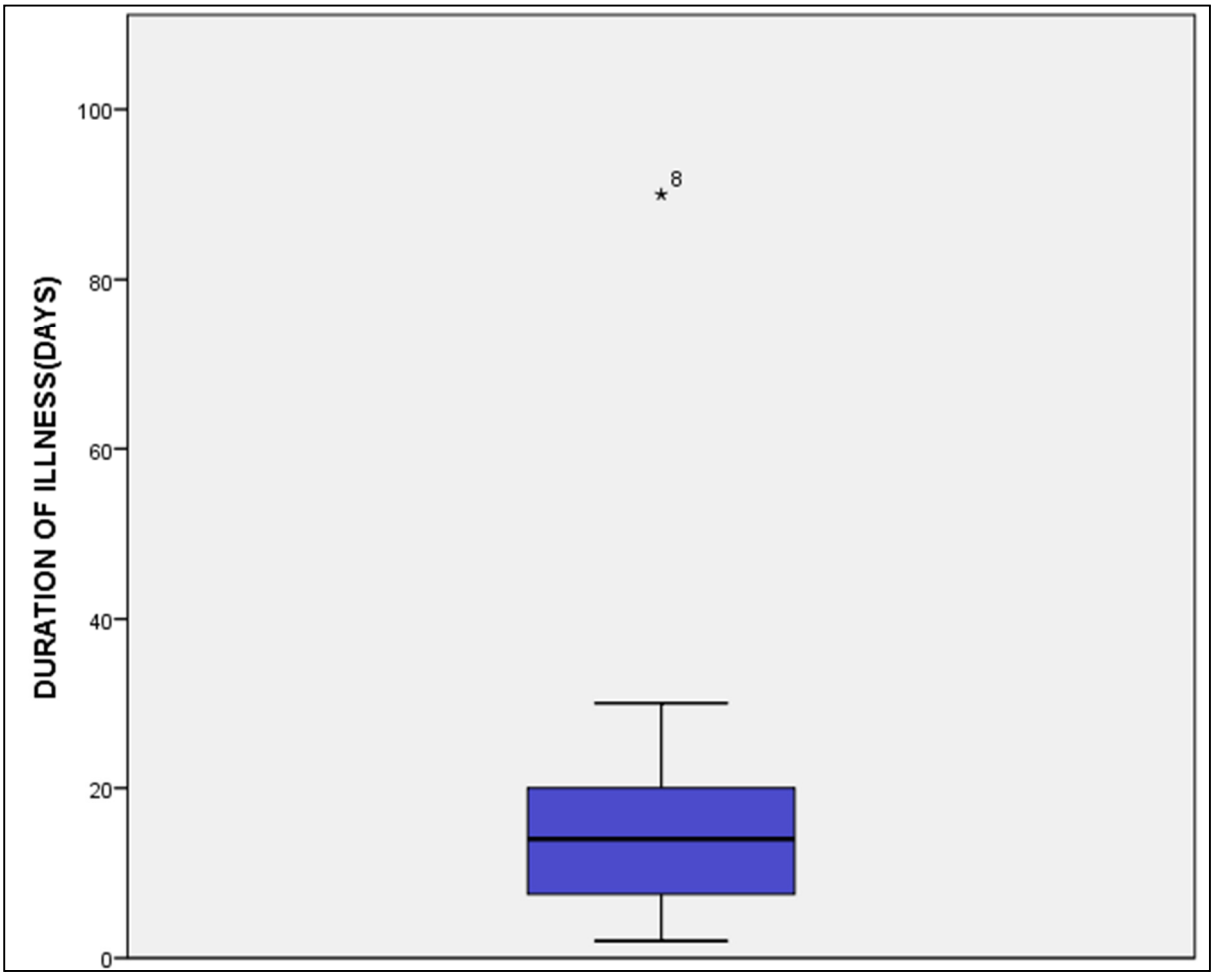


Figure 14: Box Plot showing median (IQR) (range) Duration of illness (days) in study population.

Table 8: Distribution of Time of Last Meal (in minutes) in study population

PARAMETERS	RANGE	FREQUENCY	PERCENTAGE
TIME OF LAST MEAL (min)	15-75	36	47.3
	76-135	26	34.2
	136-195	8	10.5
	196-255	5	6.5
	>255	1	1.3
	MEDIAN (IQR) (RANGE)	90 (45, 120) (15-600)	

The median (IQR) (range) time of last meal (min) in our population was 90 (45, 120) (15-600). Maximum number (47.3%) of patients had taken meal 15-75 minutes before starting on HFNC.

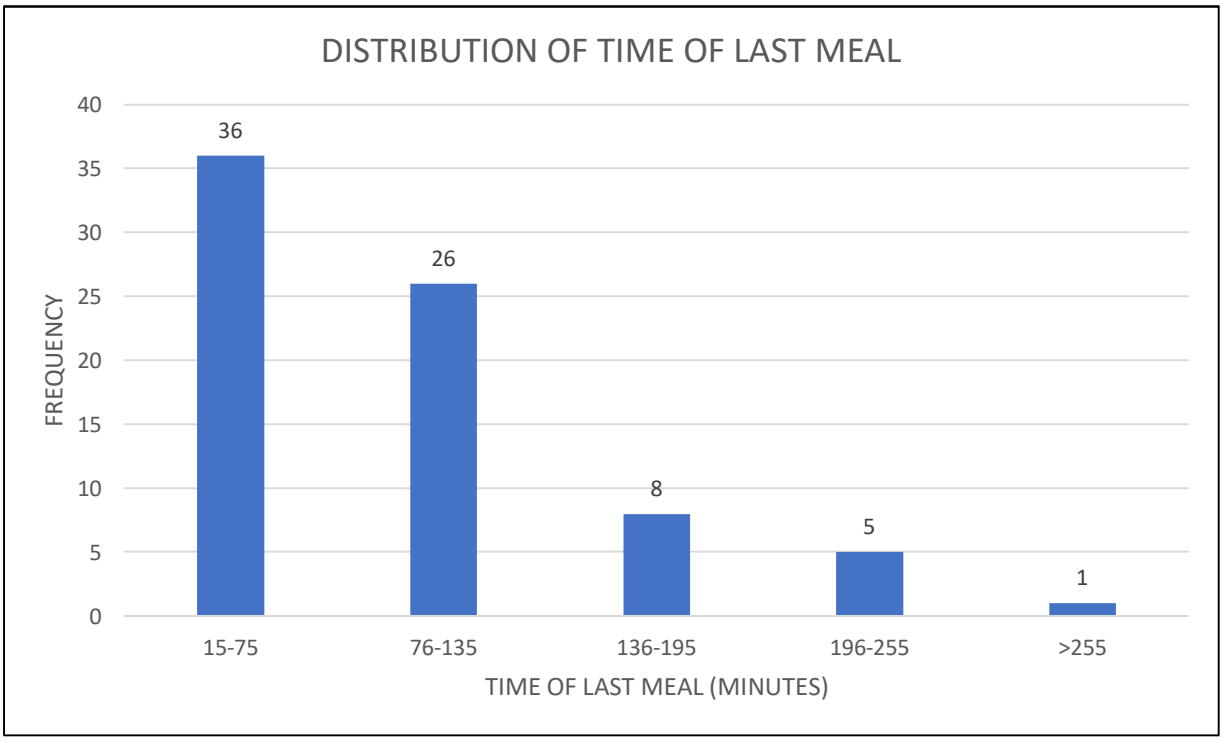


Figure 15: Bar chart showing Distribution of Time of Last Meal (in minutes) in study population

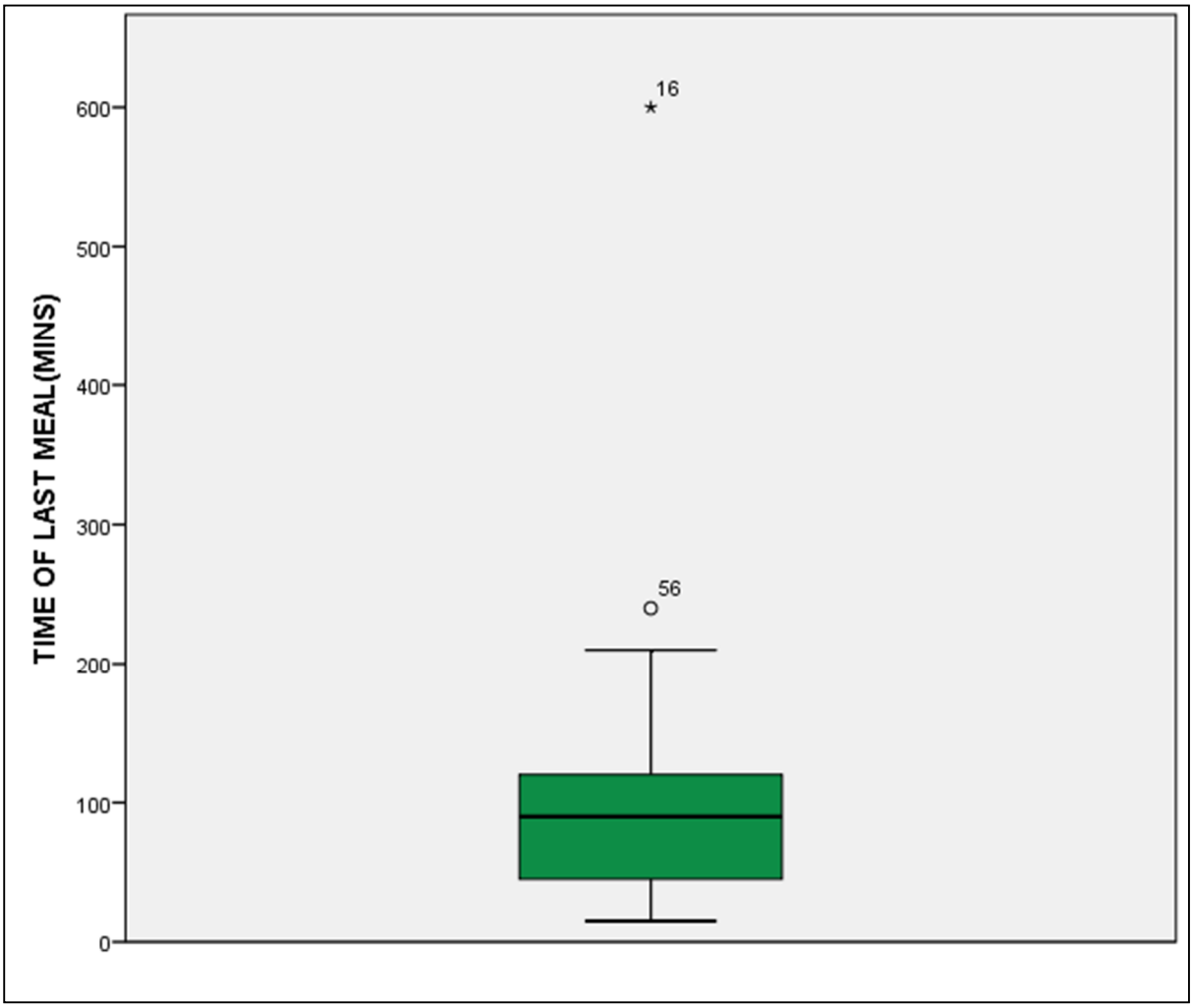


Figure 16: Box Plot showing median (IQR) (range) Time of Last Meal (min) in study population.

Table 9: Comparison of Antero-Posterior Diameter (APD) (cm) of gastric antrum before and after initiation of HFNC therapy at predefined time intervals.

PARAMETER	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
APD (cm) AT 0 MIN	2.3 (1.6, 2.9) (1.0-3.7)	-	-
APD (cm) AT 10 MIN	2.4 (1.9, 2.8) (1.0-3.7)	0.1 (-0.2 to 0.0)	0.67
APD (cm) AT 20 MIN	2.5 (2.1, 3.0) (1.1-3.5)	0.2 (-0.3 to -0.0)	0.045
APD (cm) AT 30 MIN	2.6 (1.9, 3.1) (1.5-3.9)	0.3 (-0.4 to -0.1)	0.003

The above table shows that the median (IQR) (range) APD of gastric antrum (cm) at 0, 10, 20 and 30 minutes were 2.3 (1.6, 2.9) (1.0-3.7), 2.4 (1.9, 2.8) (1.0-3.7), 2.5 (2.1, 3.0) (1.1- 3.5), and 2.6 (1.9, 3.1) (1.5-3.90) respectively. Wilcoxon signed rank test was applied to compare the APD at 10, 20 and 30 min with APD at 0 min which showed a median difference (95% CI) of 0.1 (-0.2 to 0.0), 0.2 (-0.3 to -0.0) and 0.3 (-0.4 to -0.1) respectively. The APD at 20 and 30 min was significantly larger (p-value 0.045 and 0.003 respectively) compared to APD at 0 min while there was no significant difference (p-value = 0.67) between APD at 0 min and 10 min.

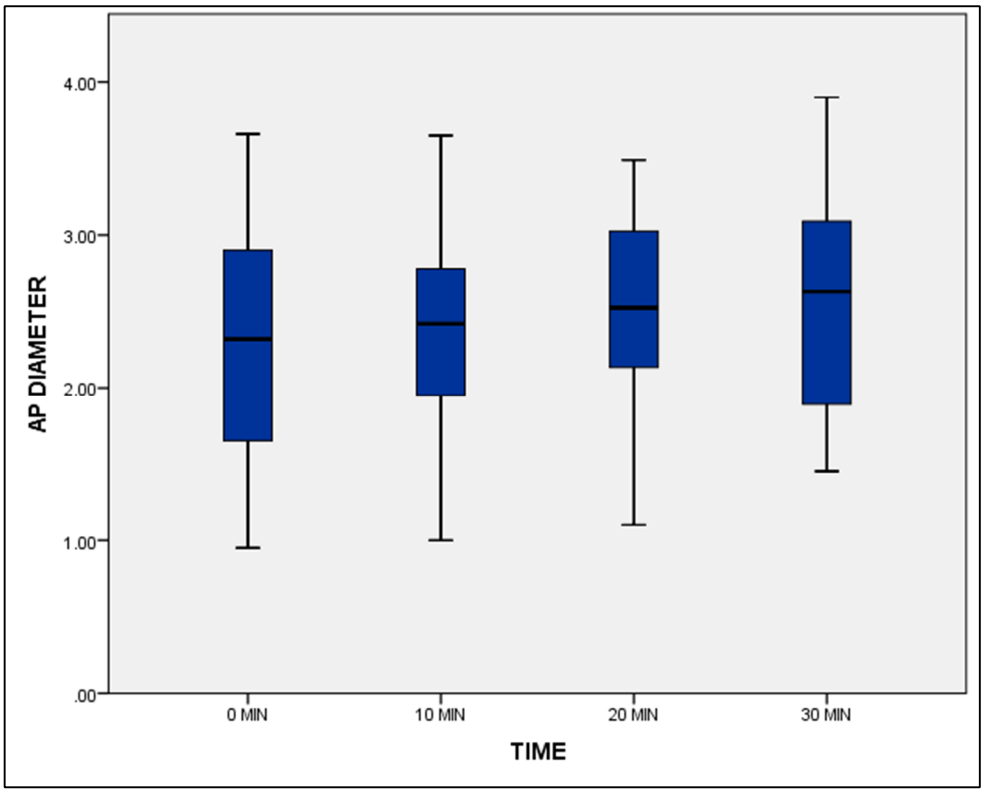


Figure 17: Box Plot showing median (IQR) (range) APD of gastric antrum (cm) before (0 min) and after (10, 20 and 30 min) initiation of HFNC therapy.

Table 10: Comparison of Transverse Diameter (TVD) of gastric antrum (cm) before and after initiation of HFNC therapy at predefined time intervals.

PARAMETER	MEDIAN (IQR) RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
TVD (cm) AT 0 MIN	2.2 (2.0, 2.4) (1.6-3.0)	-	-
TVD (cm) AT 10 MIN	2.6 (2.3, 3.0) (1.7-4.6)	0.36 (-0.7 to -0.4)	<0.0001
TVD (cm) AT 20 MIN	2.7 (2.4, 3.2) (1.8-3.9)	0.46 (-0.7 to -0.4)	<0.0001
TVD (cm) AT 30 MIN	2.6 (2.2, 3.1) (1.6-4.6)	0.4 (-0.6 to -0.3)	<0.0001

The above table shows that the median (IQR) (range) TVD of gastric antrum (cm) at 0, 10, 20 and 30 minutes were 2.2 (2.0, 2.4) (1.6-3.0), 2.6 (2.3, 3.0) (1.7-4.6), 2.7 (2.4, 3.2) (1.8-3.9), and 2.6 (2.2, 3.1) (1.6-4.6) respectively. Wilcoxon signed rank test was applied to compare the TVD at 10, 20 and 30 min with TVD at 0 min which showed a median difference (95% CI) of 0.36 (-0.7 to -0.4), 0.46 (-0.7 to -0.4) and 0.4 (-0.6 to -0.3) respectively. The TVD at 10, 20 and 30 min was significantly larger (p-value <0.0001, <0.0001 and <0.0001 respectively) compared to TVD at 0 min.

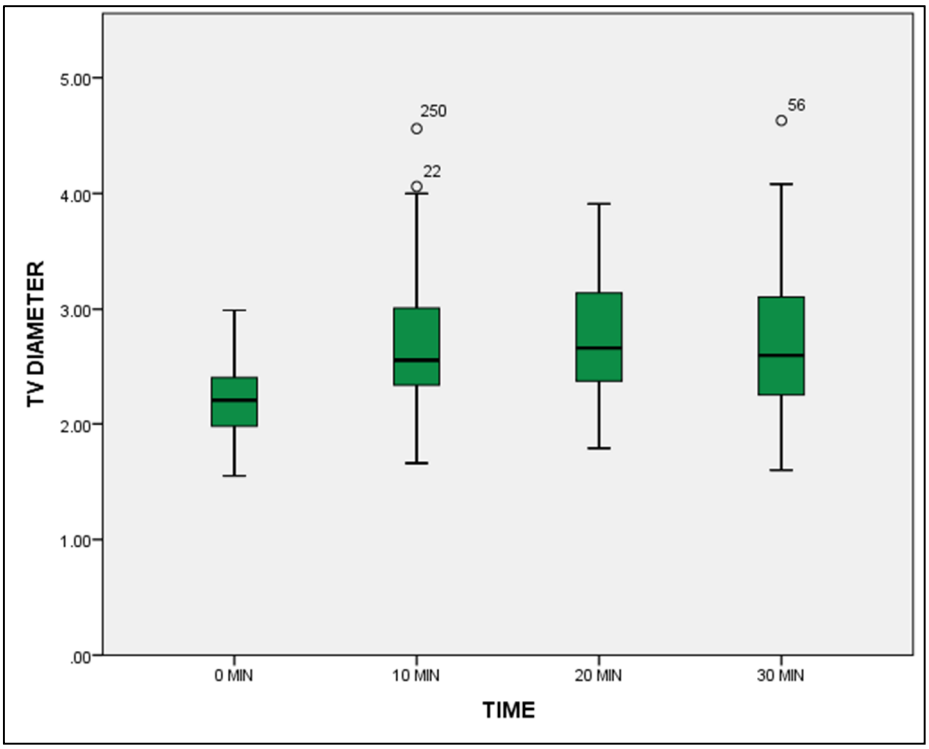


Figure 18: Box Plot showing median (IQR) (range) TVD of gastric antrum (cm) before (0 min) and after (10, 20 and 30 min) initiation of HFNC therapy.

Table 11: Comparison of Antral Cross-sectional Area (ACSA) of gastric antrum (cm^2) before and after initiation of HFNC therapy at predefined time intervals.

PARAMETER	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
ACSA (cm^2) AT 0 MIN	400.2 (279.6, 463.0) (135.2-856.2)	-	-
ACSA (cm^2) AT 10 MIN	483.4 (380.7, 695.7) (158.9-1109.7)	83.21 (-158.2 to -77.3	<0.0001
ACSA (cm^2) AT 20 MIN	501.5 (392.5, 663.8) (194.6-936.9)	101.27 (-172.6 to -95.5)	<0.0001
ACSA (cm^2) AT 30 MIN	483.6 (332.6,776.5) (225.7-1406.6)	83.38 (-212.5 to -104.5)	<0.0001

The above table shows that the median (IQR) (range) ACSA of gastric antrum (cm) at 0, 10, 20 and 30 minutes were 400.2 (279.6, 463) (135.2-856.2), 483.4 (380.7, 695.7) (158.9-1109.7), 501.5 (392.5, 663.8) (194.6-936.9), and 483.6 (332.6, 776.5) (225.7-1406.6) respectively. Wilcoxon signed rank test was applied to compare the ACSA at 10, 20 and 30 min with ACSA at 0 min which showed a median difference (95% CI) of 83.21 (-158.2 to -77.3), 101.27 (-172.6 to -95.5) and 83.38 (-212.5 to -104.5) respectively. The ACSA at 10, 20 and 30 min was significantly larger (p-value <0.0001, <0.0001 and <0.0001 respectively) compared to ACSA at 0 min.

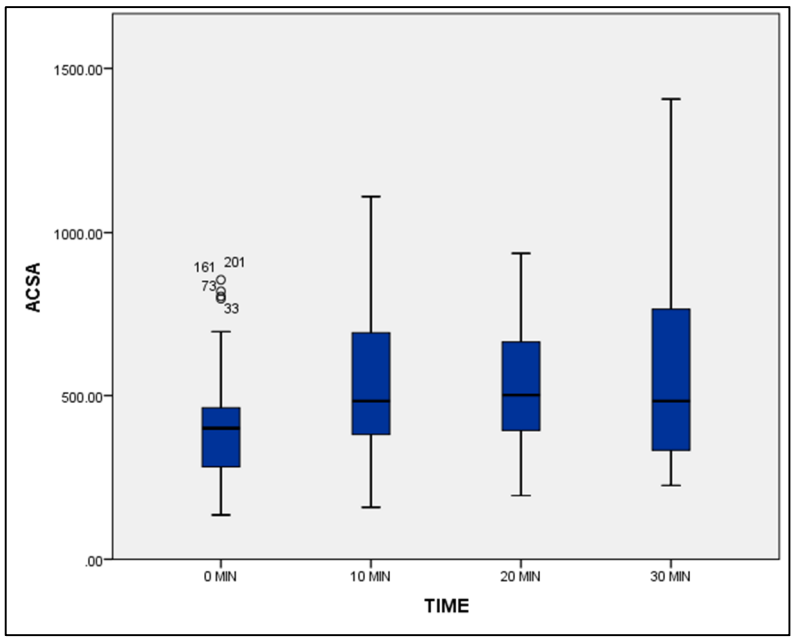


Figure 19: Box Plot showing median (IQR) (range) ACSA of gastric antrum (cm^2) before (0 min) and after (10, 20 and 30 min) initiation of HFNC therapy.

Table 12: Comparison of Gastric Volume (GV) (ml) before and after initiation of HFNC therapy at predefined time intervals.

PARAMETER	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
GV (ml) AT 0 MIN	51.9 (37.9, 68.9) (0.3-118.8)	-	-
GV (ml) AT 10 MIN	64.9 (45.4, 88.3) (0.2-131.4)	13.0 (-17.7 to -9.6)	<0.0001
GV (ml) AT 20 MIN	69.2 (50.1, 86.6) (12.0-127.3)	17.3 (-21 to 11.9)	<0.0001
GV (ml) AT 30 MIN	63.0 (42.0, 93.9) (2.1-138.2)	11.1 (-23 to -10.7)	<0.0001

The above table shows that the median (IQR) (range) GV (ml) at 0, 10, 20 and 30 minutes were 51.9 (37.9, 68.9) (0.3-118.8), 64.9 (45.4, 88.3) (0.2-131.4), 69.2 (50.1, 86.6) (12-127.3), and 63.0 (42, 93.9) (2.1-138.2) respectively. Wilcoxon signed rank test was applied to compare the GV at 10, 20 and 30 min with GV at 0 min which showed a median difference (95% CI) of 13 (-17.7 to -9.6), 17.3 (-21 to 11.9) and 11.1 (-23 to -10.7) respectively. The GV at 10, 20 and 30 min was significantly larger (p-value <0.0001, <0.0001 and <0.0001 respectively) compared to GV at 0 min.

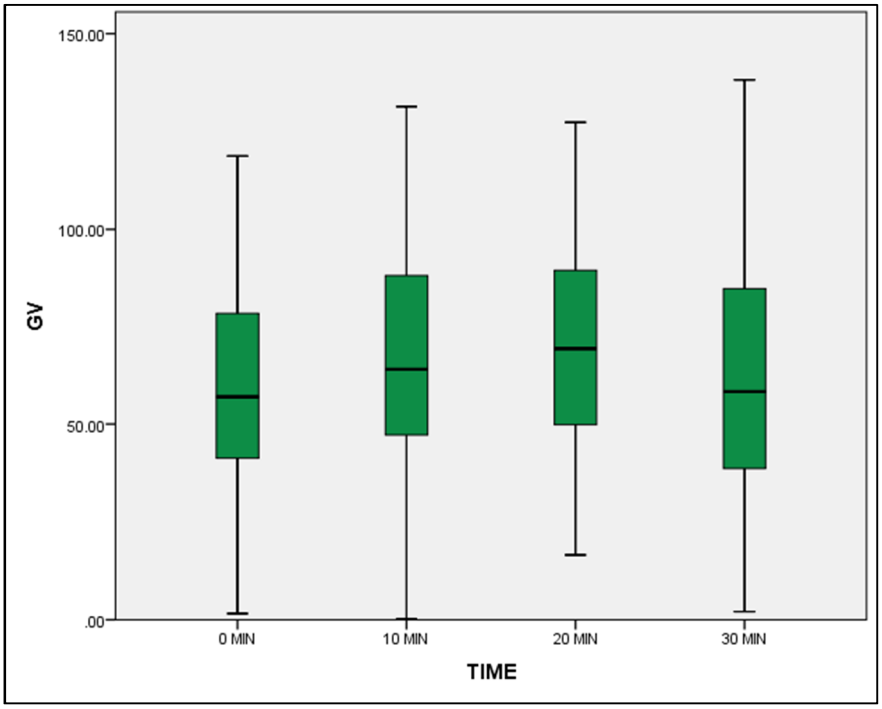


Figure 20: Box Plot showing median (IQR) (range) gastric volume (GV) (ml) before (0 min) and after (10, 20 and 30 min) initiation of HFNC therapy.

Table 13: Correlation between HFNC flow (L/min) and number of patients with increase in Gastric Volume in the study population.

FLOW (L/min)	NUMBER OF PATIENTS WITH CORRESPONDING FLOW	NUMBER OF PATIENTS WITH GV INCREASE	r coefficient 0.541
30	11	0	
40	19	13	p-value
50	22	18	<0.0001
60	24	22	

The above table shows that there was a higher occurrence of gastric volume increase among patients with higher flows of HFNC. The Spearman correlation coefficient was calculated to find out the correlation between HFNC flow and number of patients with increase in GV. There was a significant positive correlation (r=0.541) (p=<0.0001) between HFNC flow and increase in gastric volume.

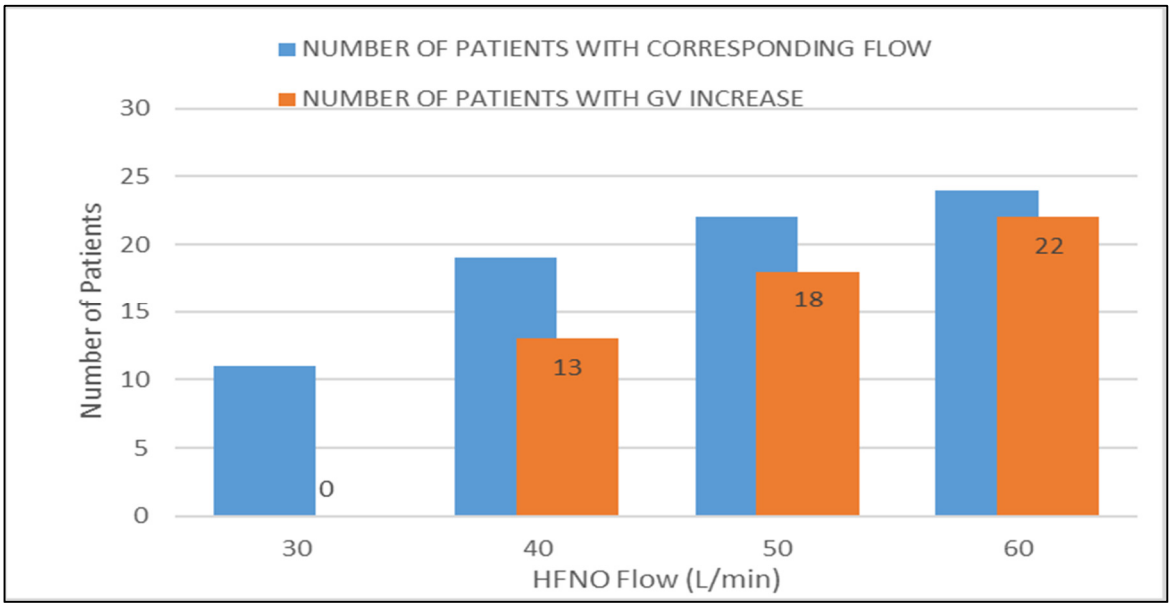


Figure 21: Bar chart showing number of patients at different HFNC flows and number of patients who had an increase in gastric volume at that particular flow.

Table 14: Comparison of number of patients with GV>0.8 ml/kg at 0 minute and 30 minutes

TIME(MINS)	NUMBER OF PATIENTS WITH GV<0.8 ML/KG	NUMBER OF PATIENTS WITH GV>0.8 ML/KG
AT 0 MIN	60	16
AT 30 MIN	31	45

The gastric volume calculated in the study population at 0 min after application of HFNC was more than 0.8 ml/kg in 16 patients (21%). This number increased to 45 patients (59%) after 30 minutes of application of HFNC.

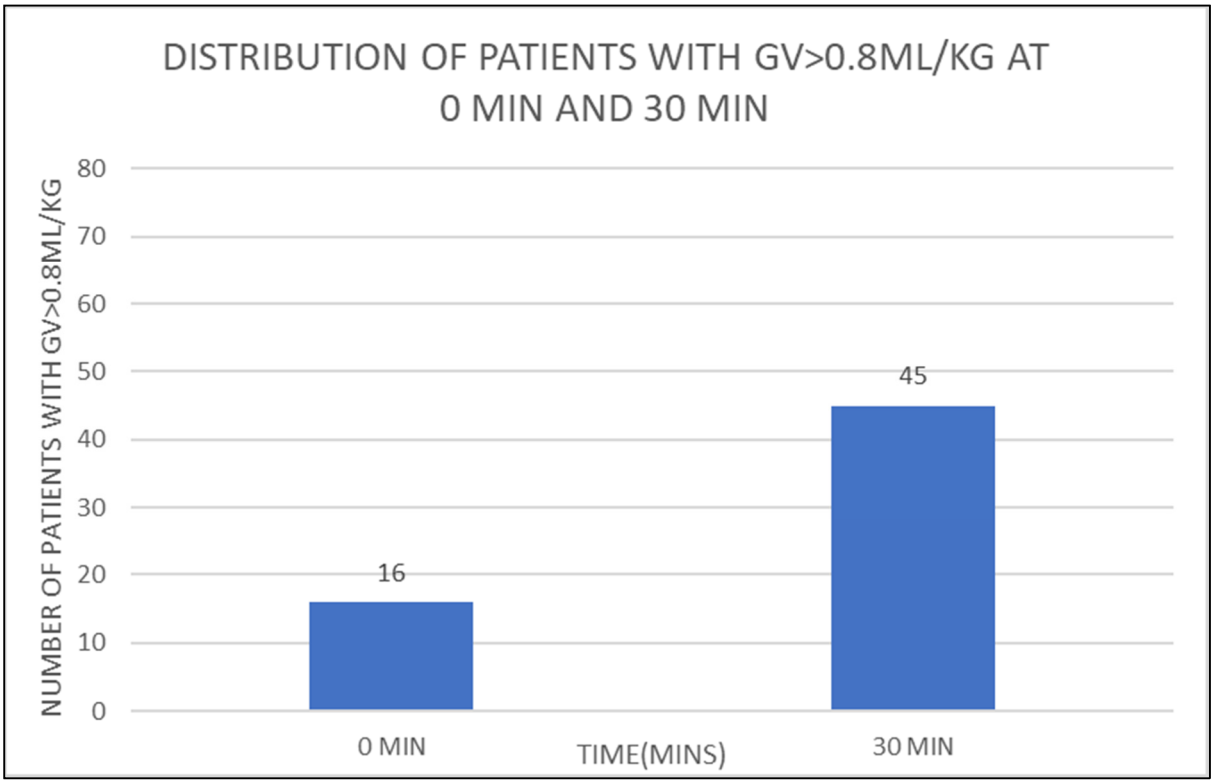


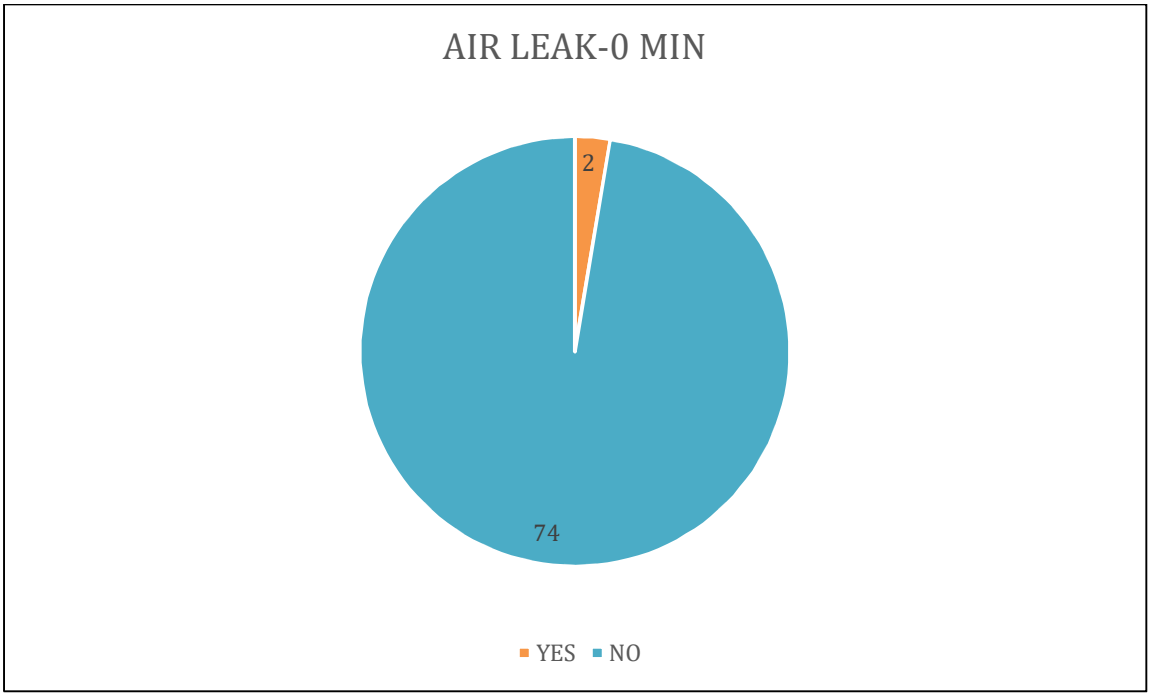
Figure 22: Bar chart showing Distribution of patients with Gastric Volume >0.8 ml/kg in the study population at 0 min and 30 min

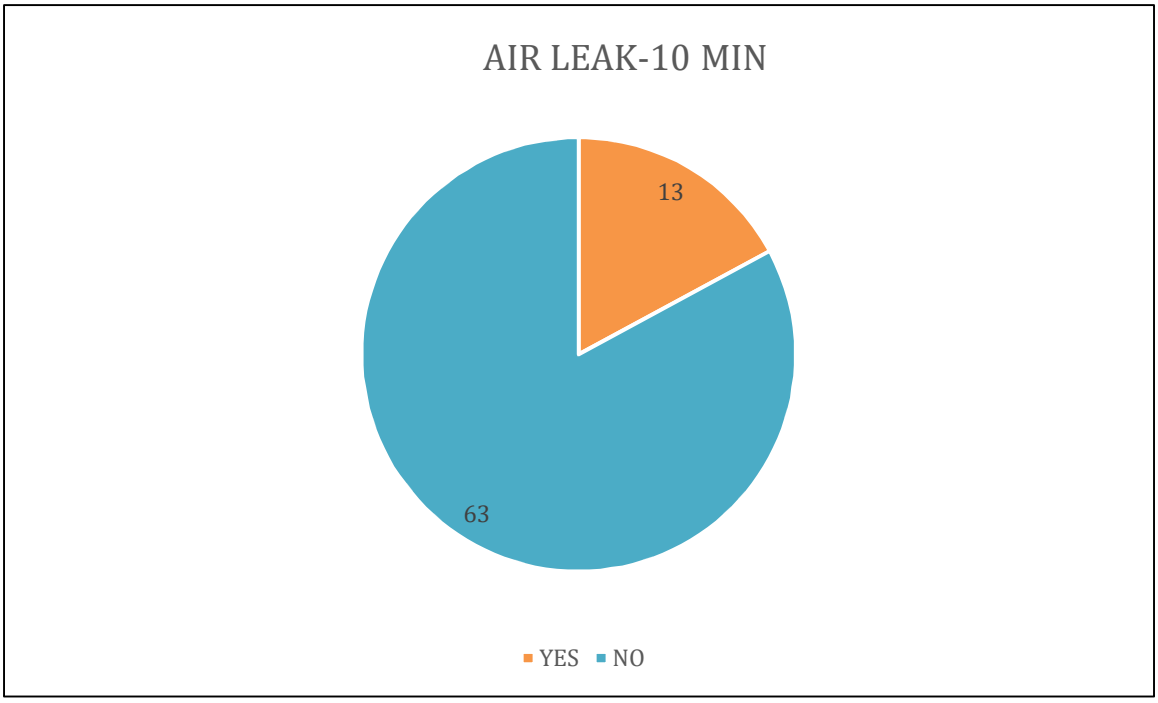
Table 15: Comparison of Air leak at predefined time intervals after initiation of HFNC.

	FREQUENCY	PERCENTAGE	p-value
AIR LEAK AT 0 MIN	2	2.6	-
AIR LEAK AT 10 MIN	13	17.1	0.001
AIR LEAK AT 20 MIN	41	53.9	<0.0001
AIR LEAK AT 30 MIN	46	60.5	<0.0001

Out of 76 patients enrolled in the study, only 2 patients (2.6%) had air leak in gastric antrum before application of HFNC while 13 (17.1%), 41 (53.9%) and 46 (60.5%) patients had air leak at 10, 20 and 30 min respectively. Significantly higher numbers of patients had air leak at 10 min (p-value=0.001), 20 min (p-value<0.0001) and at 30 min (p-value<0.0001) compared with air leak at 0 min.

The incidence of air leak at 10 minutes, 20 minutes and 30 minutes were calculated and found to be 14%, 52% and 59% respectively.


AIR LEAK-0 MIN
2
74
YES
NO


AIR LEAK-10 MIN
13
63
YES
NO

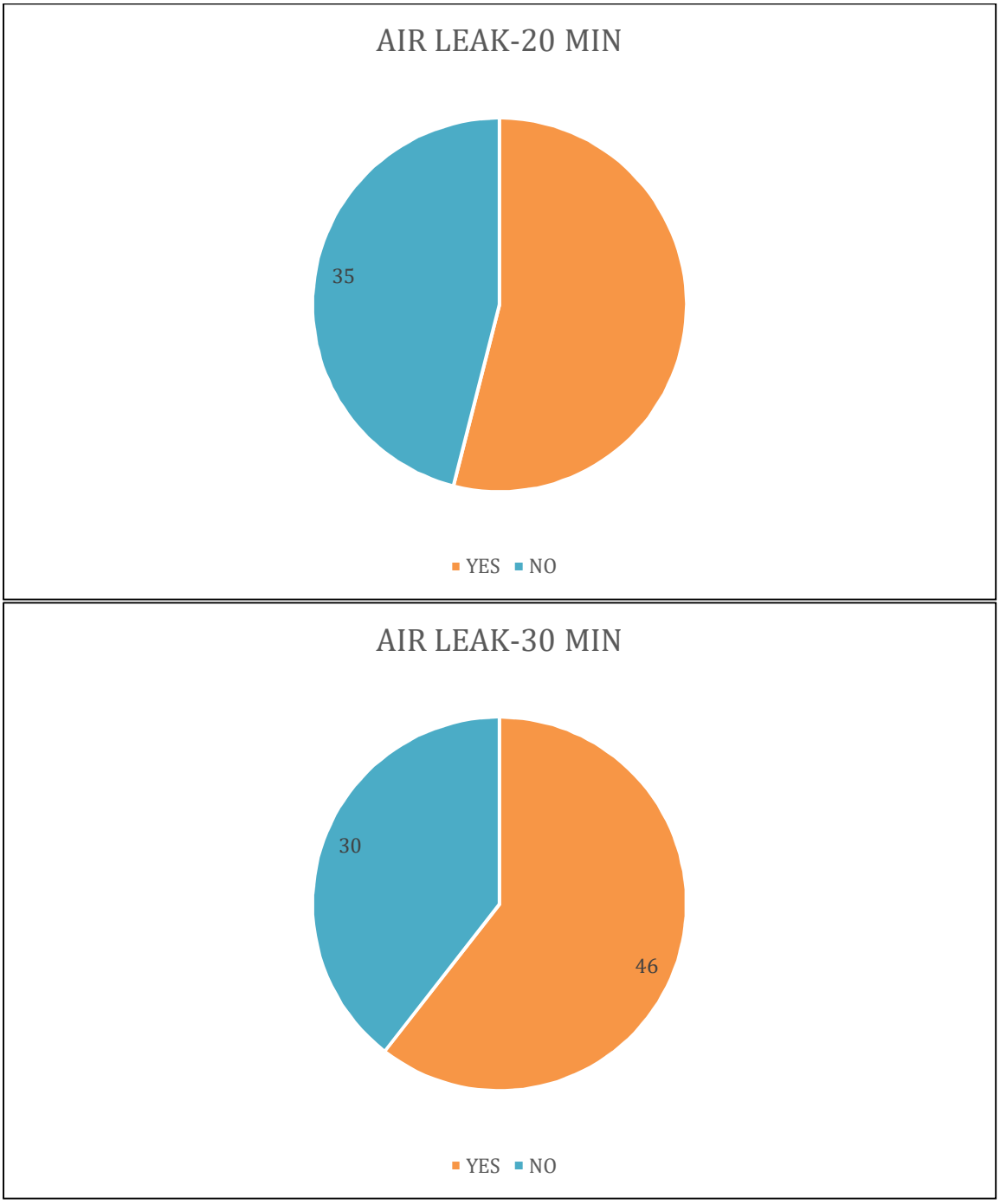


Figure 23: Pie chart showing number of patients with Air leak before and after initiation of HFNC therapy at predefined time intervals

Table 16: Comparison of Peristaltic contractions before (at 0 min) and after (at 10 min)initiation of HFNC therapy.

NUMBER OF PERISTALTIC CONTRACTIONS	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	0 (0, 2) (0-4)	-	-
AT 10 MIN	1 (0, 3) (0-7)	1 (-1.4 to -0.8)	<0.0001

The median (IQR) (range) number of peristaltic contractions at 0 and 10 min was 0 (0, 2) (0-4) and 1 (0, 3) (0-7). Wilcoxon signed rank test was applied to compare the number of peristaltic contractions at two time points which showed a median difference (95% CI) of 1 (-1.4 to -0.8) and p-value <0.0001. There was a significant increase in the number of peristaltic contractions after application of HFNC.

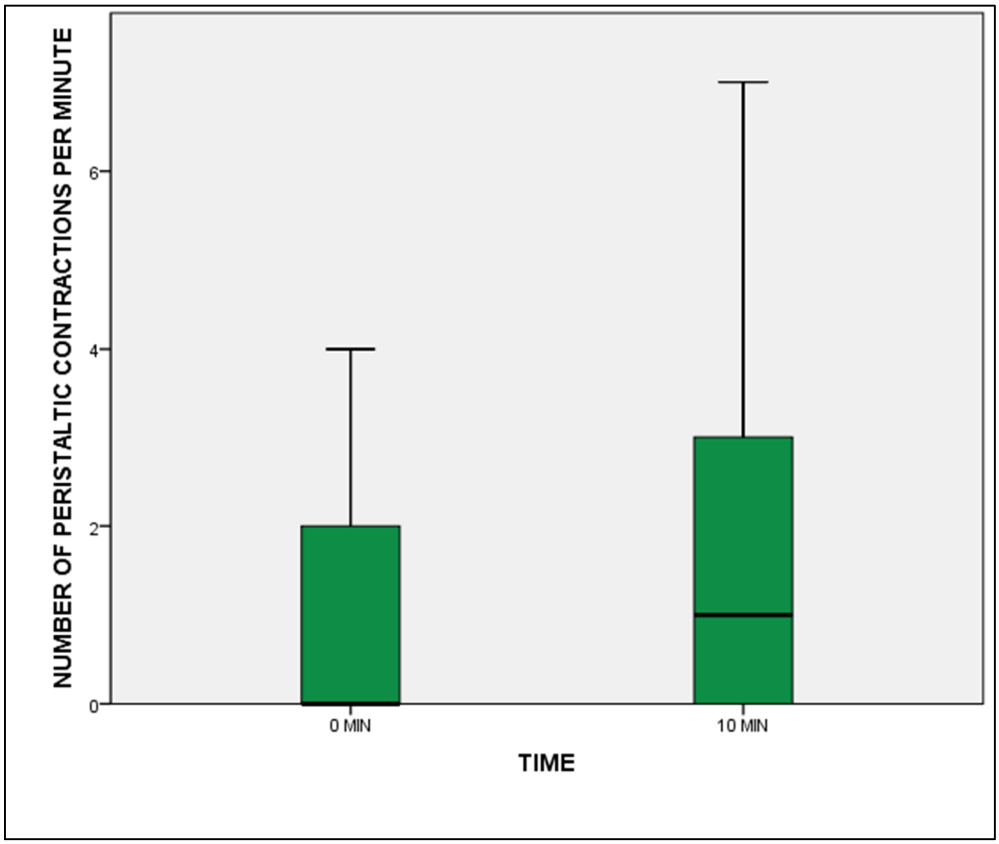


Figure 24: Box Plot showing median (IQR) (range) number of Peristaltic contractions before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 17: Comparison of Heart Rate (HR) (beats per minute) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

HEART RATE (beat per min)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	98.5 (79.8, 118) (55-134)	-	-
AT 30 MIN	99.0 (76.3, 114) (52-136)	0.5 (-0.6 to 3.9)	0.08

The median (IQR) (range) HR (beat per min) at 0 and 10 min was 98.5 (79.8, 118) (55-134) and 99 (76.3, 114) (52-136) respectively. Wilcoxon signed rank test was applied to compare the HR at two time points which showed a median difference (95% CI) of 0.5 (-0.6 to 3.9) and p-value 0.08. There was no significant change in HR after the application of HFNC.

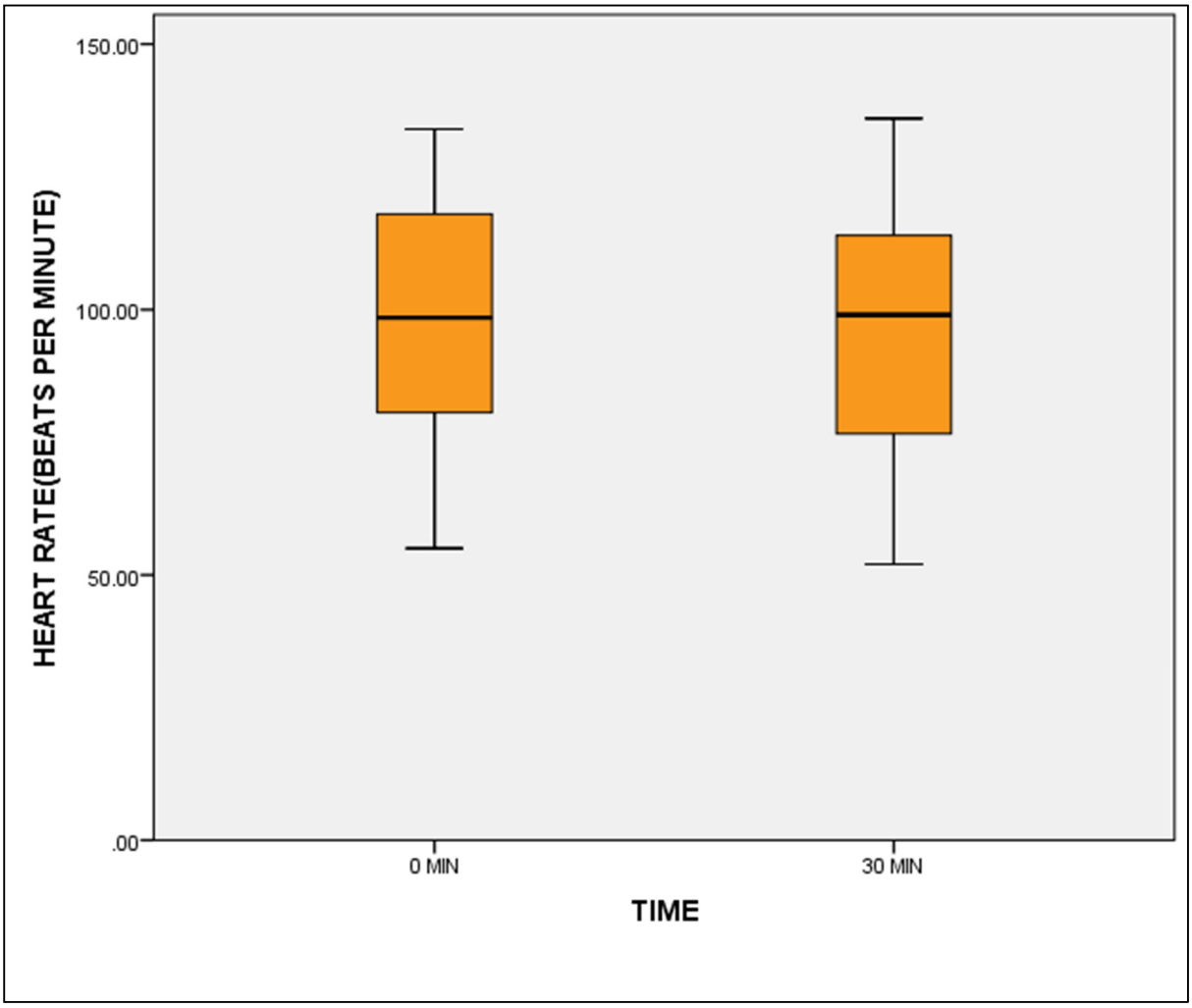


Figure 25: Box Plot showing median (IQR) (range) HR (beat per min) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 18: Comparison of Systolic Blood Pressure (SBP) (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

SYSTOLIC BLOOD PRESSURE (mmHg)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	128 (113.3, 140.8) (94-184)	-	-
AT 30 MIN	124 (114.5, 138.8) (94-178)	4 (-2.5 to 2.6)	0.43

The median (IQR) (range) SBP (mmHg) at 0 and 10 min was 128 (113.3, 140.8) (94-184) and 124 (114.5, 138.8) (94-178) respectively. Wilcoxon signed rank test was applied to compare the SBP at two time points which showed a median difference (95% CI) of 4 (-2.5 to 2.6) and p-value 0.43. There was no significant change in the SBP after the application of HFNC.

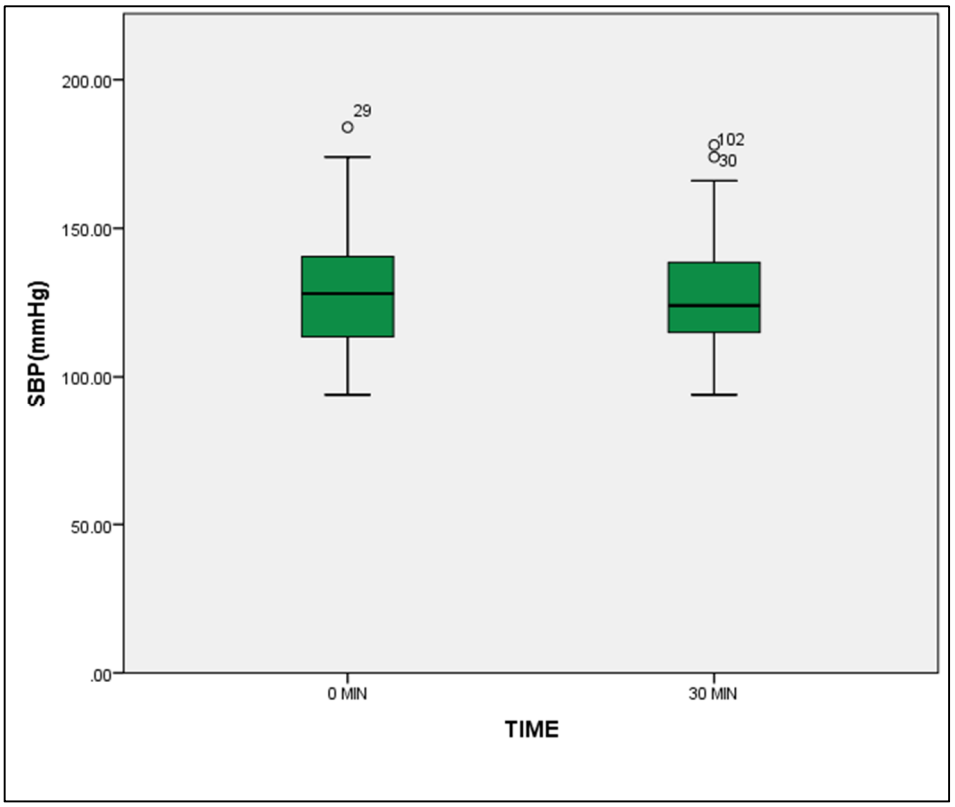


Figure 26: Box Plot showing median (IQR) (range) SBP (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 19: Comparison of Diastolic Blood Pressure (DBP) (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

DIASTOLIC BLOOD PRESSURE (mmHg)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	76 (66, 87) (47-103)	-	-
AT 30 MIN	78 (69.3, 84) (56-111)	2 (-3.1 to 1.2)	0.38

The median (IQR) (range) DBP (mmHg) at 0 and 10 min was 76 (66, 87) (47-103) and 78 (69.3, 84) (56-111) respectively. Wilcoxon signed rank test was applied to compare the DBP at two time points which showed a median difference (95% CI) of 2 (-3.1 to 1.2) and p-value 0.38. There was no significant change in the DBP after the application of HFNC.

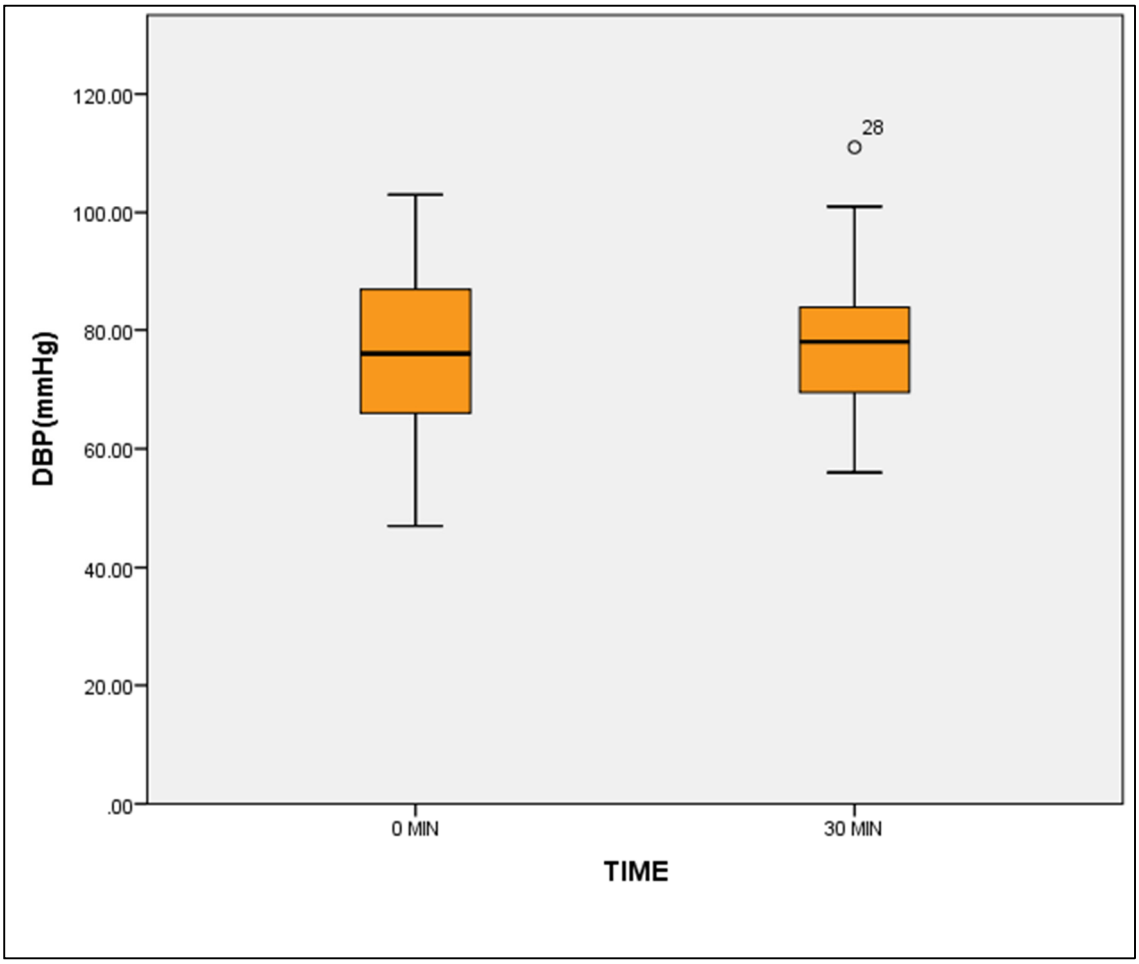


Figure 27: Box Plot showing median (IQR) (range) DBP (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 20: Comparison of Mean Blood Pressure (MBP) (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

MEAN BLOOD PRESSURE (mmHg)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	95.3 (82.2, 102.6) (68-121)	-	-
AT 30 MIN	93.3 (85.3, 103.1) (68.7-128)	2 (-2.5 to 1.3)	0.97

The median (IQR) (range) MBP (mmHg) at 0 and 10 min was 95.3 (82.2, 102.6) (68-121) and 93.3 (85.3, 103.1) (68.7-128) respectively. Wilcoxon signed rank test was applied to compare the MBP at two time points which showed a median difference (95% CI) of 2 (-2.5 to 1.3) and p-value 0.97. There was no significant change in the MBP after the application of HFNC.

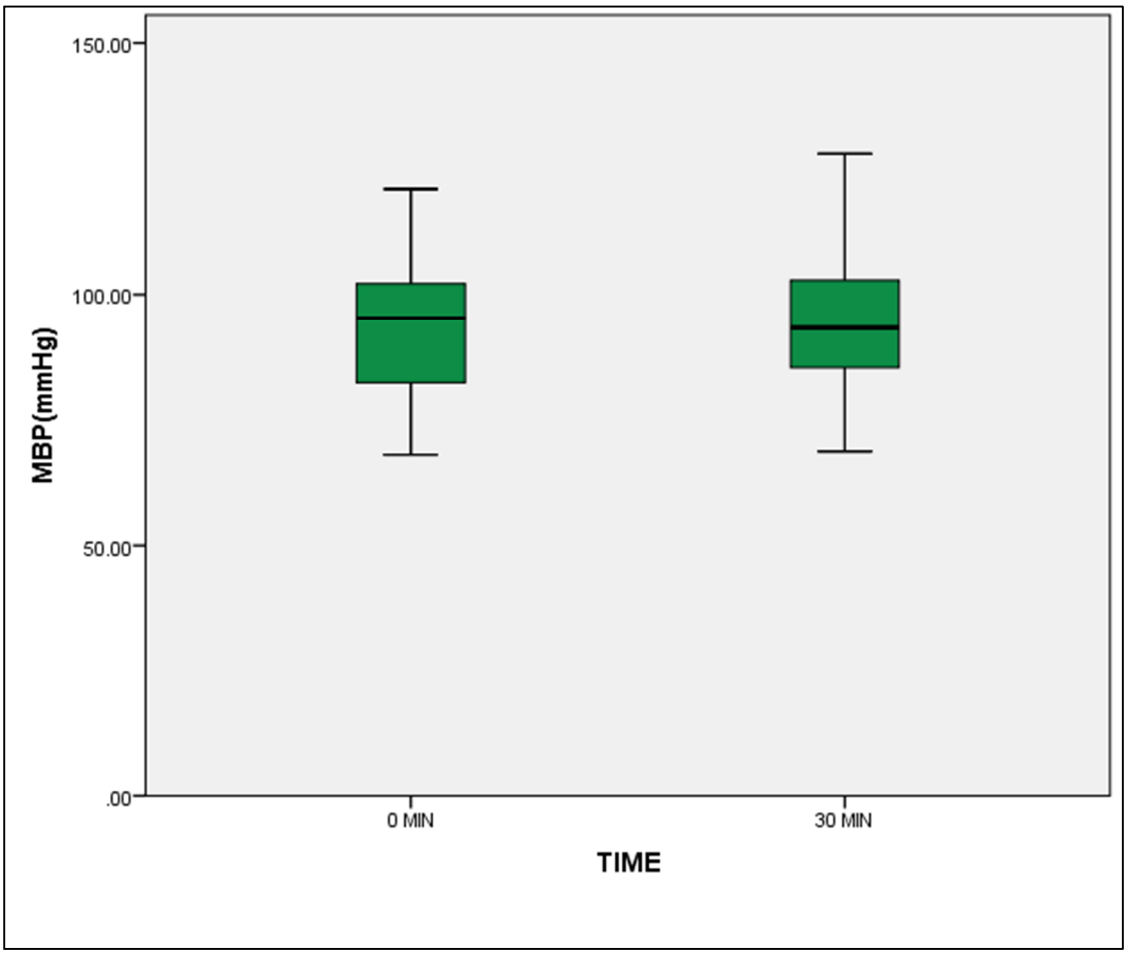


Figure 28: Box Plot showing median (IQR) (range) MBP (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 21: Comparison of Peripheral oxygen saturation (SpO_2) (%) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

PERIPHERAL OXYGEN SATURATION (SpO_2) (%)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	88 (86, 89) (80-92)	-	-
AT 30 MIN	93.5 (91, 94) (90-99)	5.5 (-5.9 to -5.0)	<0.0001

The median (IQR) (range) SpO_2 (%) at 0 and 10 min was 88 (86, 89) (80-92) and 93.5 (91, 94) (90-99) respectively. Wilcoxon signed rank test was applied to compare the SpO_2 at two time points which showed a median difference (95% CI) of 5.5 (-5.9 to -5.0) and p-value <0.0001. There was a significant increase in the SpO_2 after the application of HFNC.

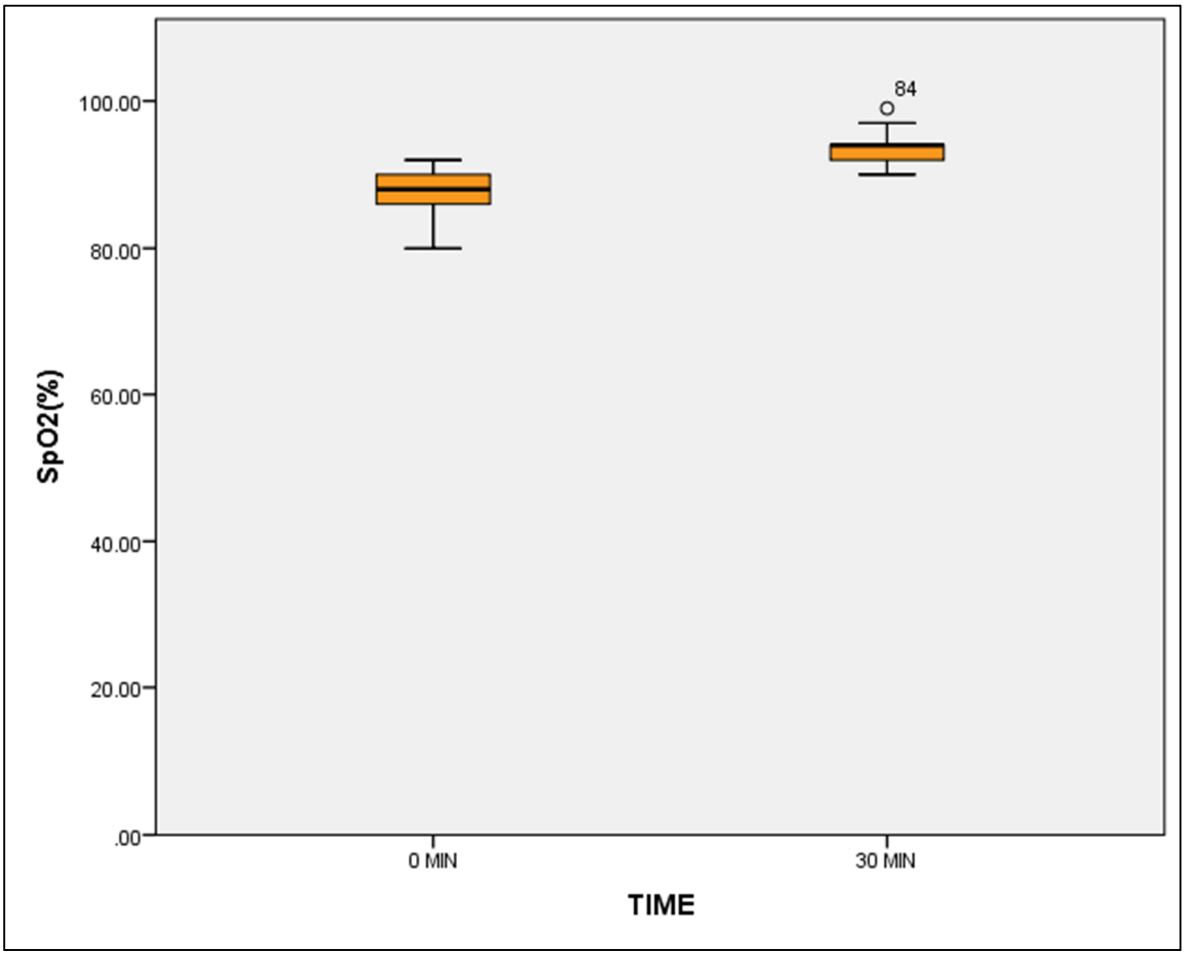


Figure 29: Box Plot showing median (IQR) (range) SpO_2 (%) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 22: Comparison of Respiratory Rate (RR) (per min) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

RESPIRATORY RATE (per min)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	30 (26, 35) (18-50)	-	-
AT 30 MIN	26 (22, 32) (18-43)	4 (2.4-3.5)	<0.0001

The median (IQR) (range) RR (per min) at 0 and 10 min was 30 (26, 35) (18-50) and 26 (22, 32) (18-43) respectively. Wilcoxon signed rank test was applied to compare the RR at two time points which showed a median difference (95% CI) of 4 (2.4-3.5) and p-value <0.0001. There was a significant decrease in the RR after the application of HFNC.

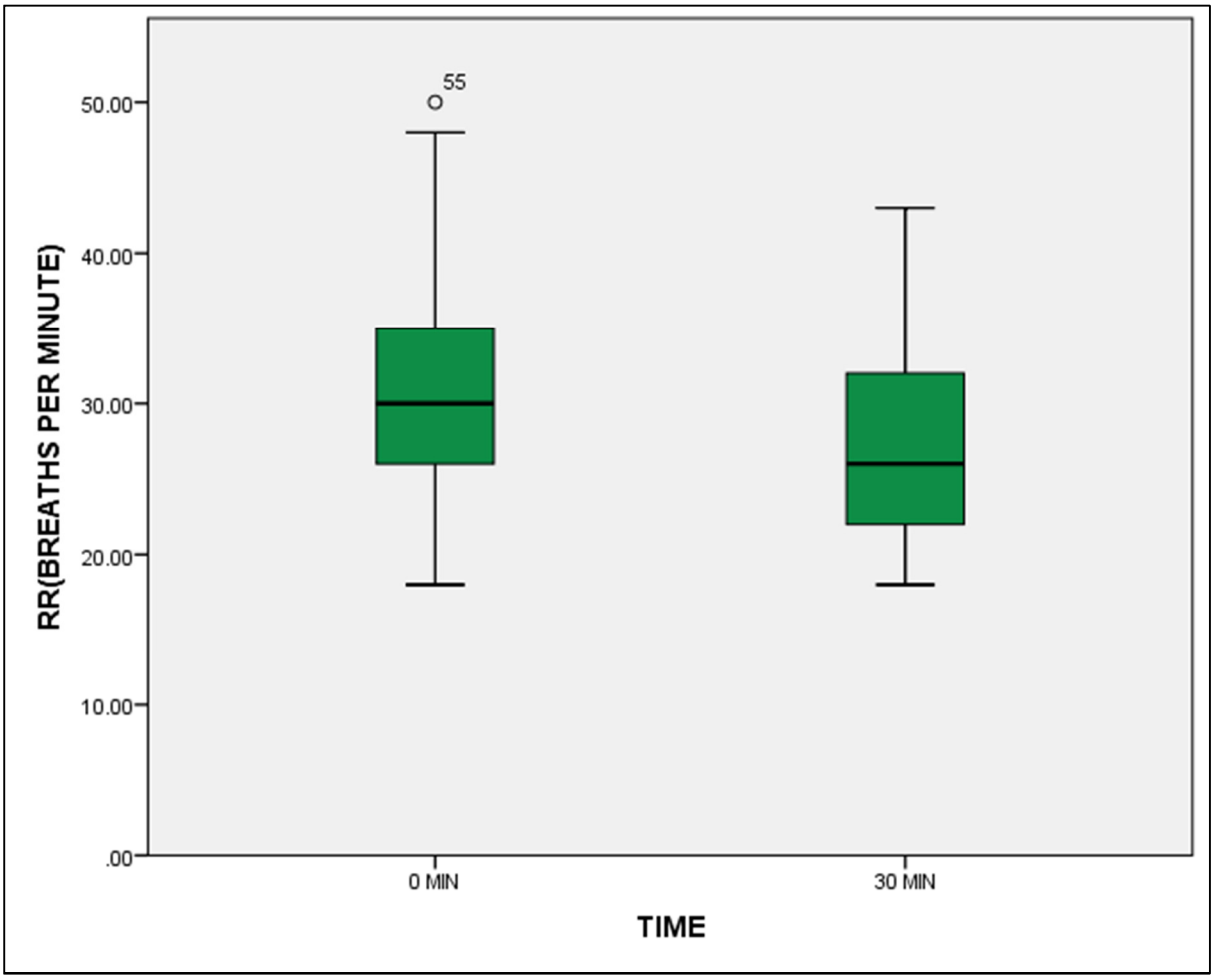


Figure 30: Box Plot showing median (IQR) (range) RR (per min) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 23: Comparison of Partial Pressure of Oxygen in the arterial blood (PaO_2) (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

PaO_2 (mmHg)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	71.7 (65.2, 78) (52.4-102.8)	-	-
AT 30 MIN	78.6 (70.3-87.5) (58.6-168)	6.9 (-12.6 to -6.7)	<0.0001

The median (IQR) (range) PaO_2 (mmHg) at 0 and 10 min was 71.7 (65.2, 78) (52.4-102.8) and 78.6 (70.3-87.5) (58.6-168) respectively. Wilcoxon signed rank test was applied to compare the PaO_2 at two time points which showed a median difference (95% CI) of 6.9 (-12.6 to -6.7) and p-value <0.0001. There was a significant increase in the PaO_2 after the application of HFNC.

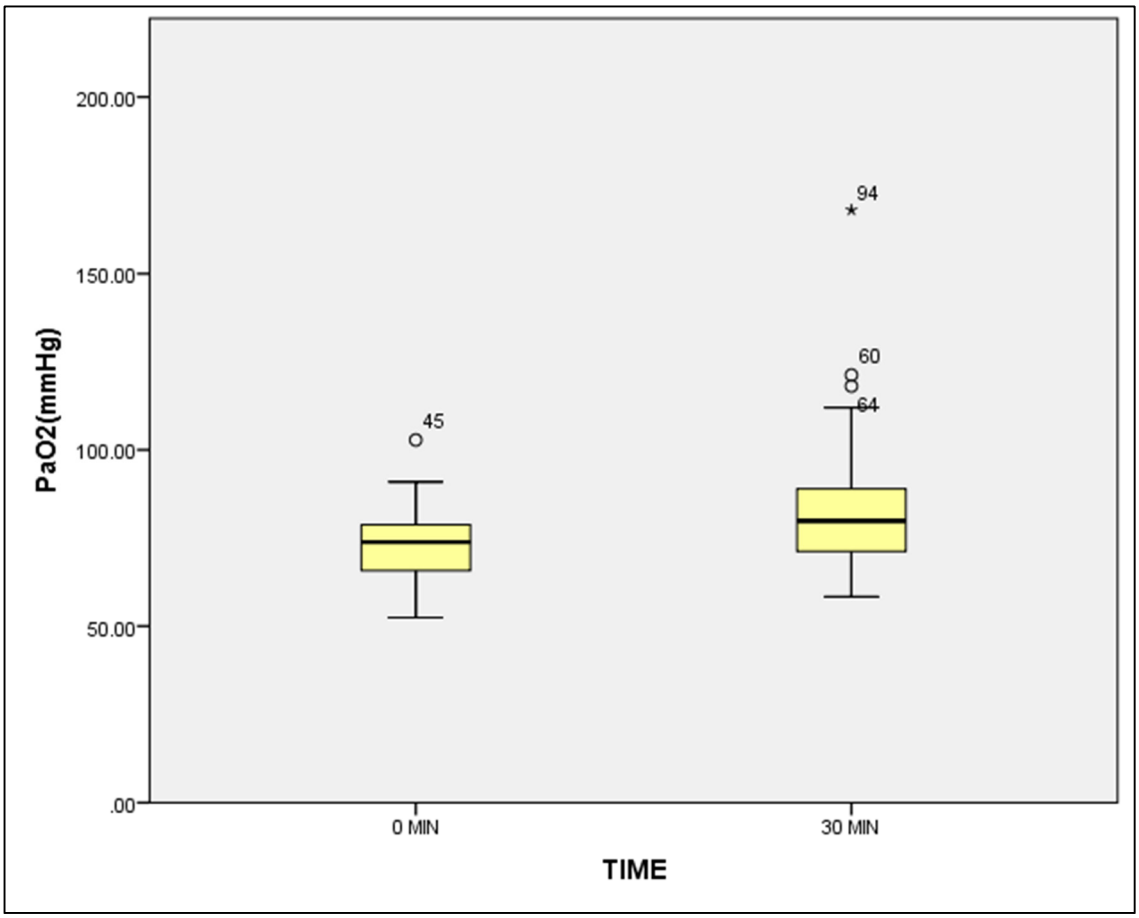


Figure 31: Box Plot showing median (IQR) (range) PaO_2 (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 24: Comparison of Partial Pressure of Carbon Dioxide in the arterial blood ($PaCO_2$) (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

$PaCO_2$ (mmHg)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	41.6 (39, 45) (23.4-78.6)	-	-
AT 30 MIN	40 (37.9, 44.1) (23.6-75)	1.6 (0.6-1.5)	<0.0001

The median (IQR) (range) $PaCO_2$ (mmHg) at 0 and 10 min was 41.6 (39, 45) (23.4-78.6) and 40 (37.9, 44.1) (23.6-75) respectively. Wilcoxon signed rank test was applied to compare the $PaCO_2$ at two time points which showed a median difference (95% CI) of 1.6 (0.6-1.5) and p-value <0.0001. There was a significant decrease in the $PaCO_2$ after the application of HFNC.

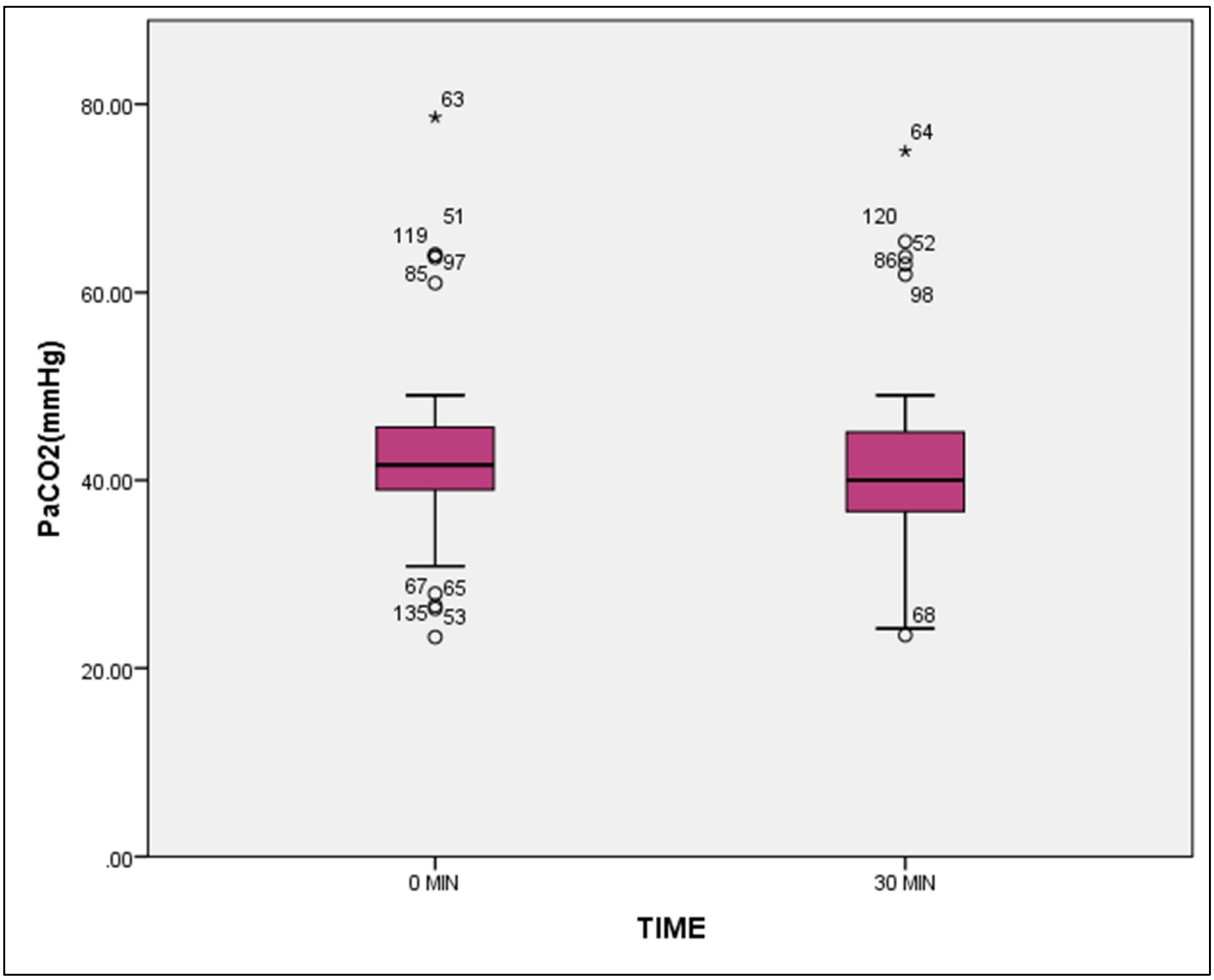


Figure 32: Box Plot showing median (IQR) (range) $PaCO_2$ (mmHg) before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 25: Comparison of ratio of PaO_2 and FiO_2 (PF-ratio) in the arterial blood before (at 0 min) and after (at 10 min) initiation of HFNC therapy

PF RATIO	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	108.3 (93, 134.5) (52.4-211.4)	-	-
AT 30 MIN	120.4 (100.0, 158.9) (58.6-281.3)	12.1 (-23.9 to -11)	<0.0001

The median (IQR) (range) PF-ratio at 0 and 10 min was 108.3 (93, 134.5) (52.4-211.4) and 120.4 (100.0, 158.9) (58.6-281.3) respectively. Wilcoxon signed rank test was applied to compare the PF-ratio at two time points which showed a median difference (95% CI) of 12.1 (-23.9 to -11) and p-value <0.0001. There was a significant increase in the PF-ratio after the application of HFNC.

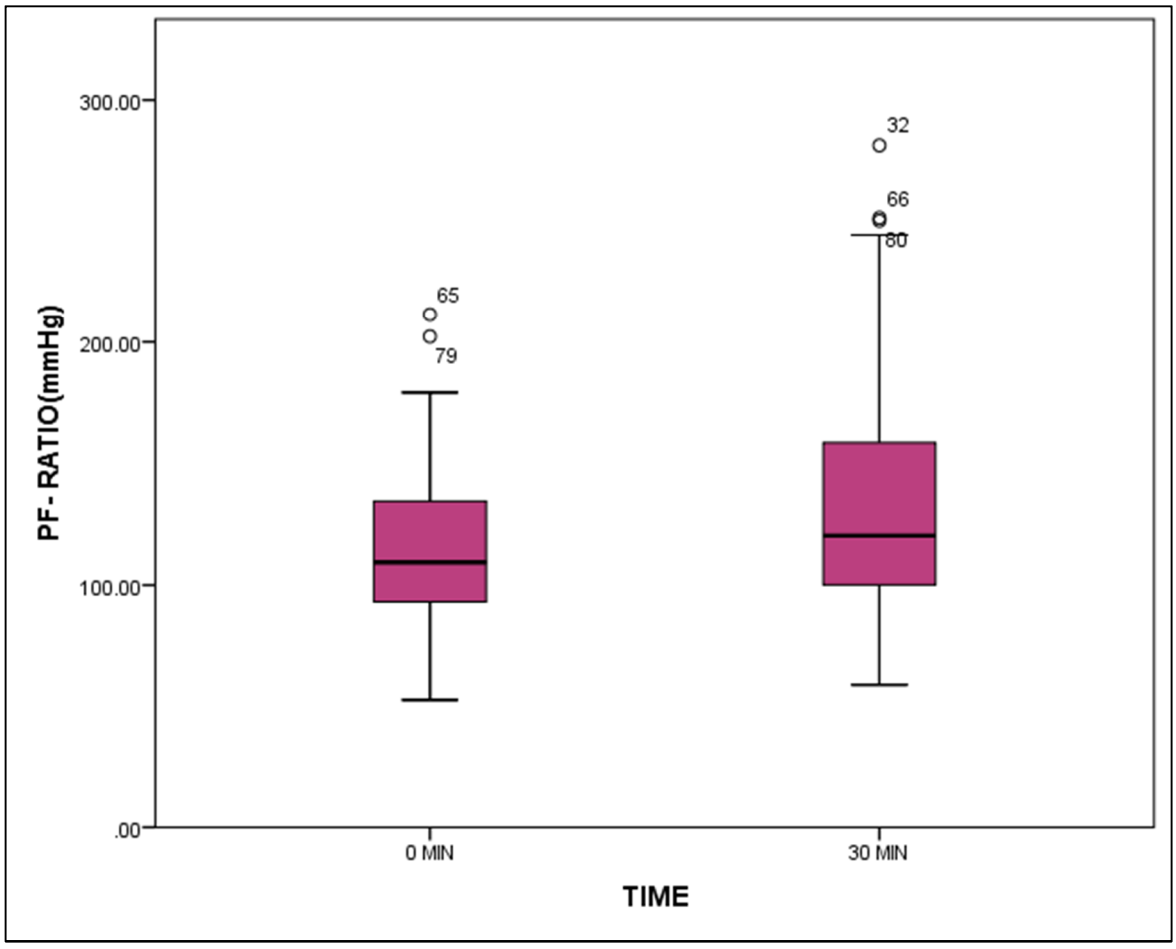


Figure 33: Box Plot showing median (IQR) (range) PF-ratio before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 26: Comparison of ratio of Arterial Oxygen Saturation (SaO_2) (%) before (at 0 min) and after (at 10 min) initiation of HFNC therapy

SaO_2 (%)	MEDIAN (IQR) (RANGE)	MEDIAN DIFF (95% CI) COMPARED TO BASELINE	p-value
AT 0 MIN	88 (85.6, 88) (80.9-93.9)	-	-
AT 30 MIN	91 (89.6, 92) (86-97.1)	3 (-4 to -3.1)	<0.0001

The median (IQR) (range) SaO_2 at 0 and 10 min was 88 (85.6, 88) (80.9-93.9) and 91 (89.6, 92) (86-97.1) respectively. Wilcoxon signed rank test was applied to compare the PF-ratio at two time points which showed a median difference (95% CI) of 3 (-4 to -3.1) and p-value <0.0001. There was a significant increase in the SaO_2 after the application of HFNC.

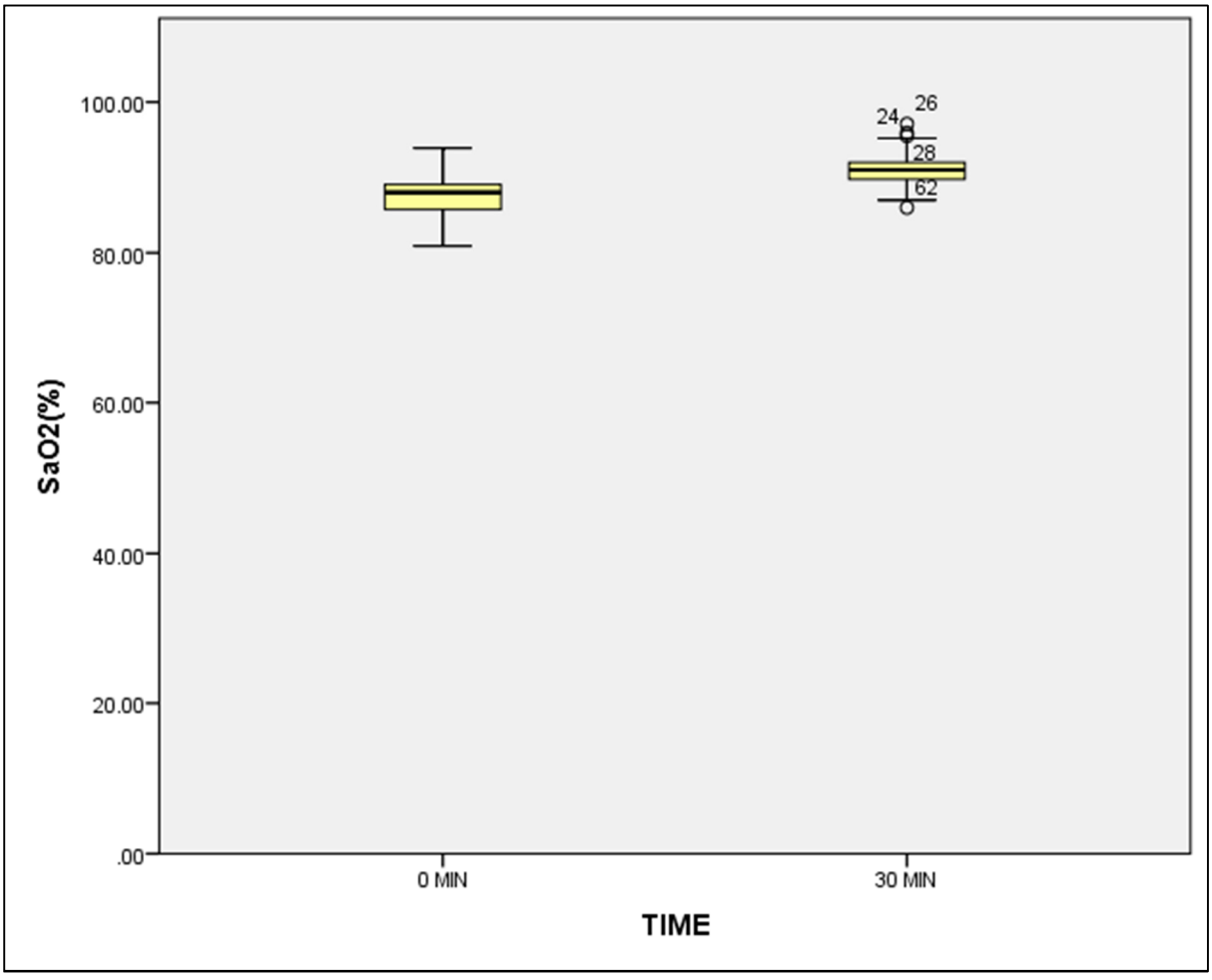


Figure 34: Box Plot showing median (IQR) (range) SaO_2 before (at 0 min) and after (at 10 min) initiation of HFNC therapy.

Table 27: Complaints of Nausea or vomiting

PARAMETER		FREQUENCY	PERCENTAGE
COMPLAINTS OF NAUSEA OR VOMITING	NO	69	90.8
	YES	7	9.2

The above table shows that only 7 patients (9.2%) of the study population complained of nausea or vomiting after 30 mins of HFNC therapy. 69 patients (90.8%) of the patients were free of any symptoms.

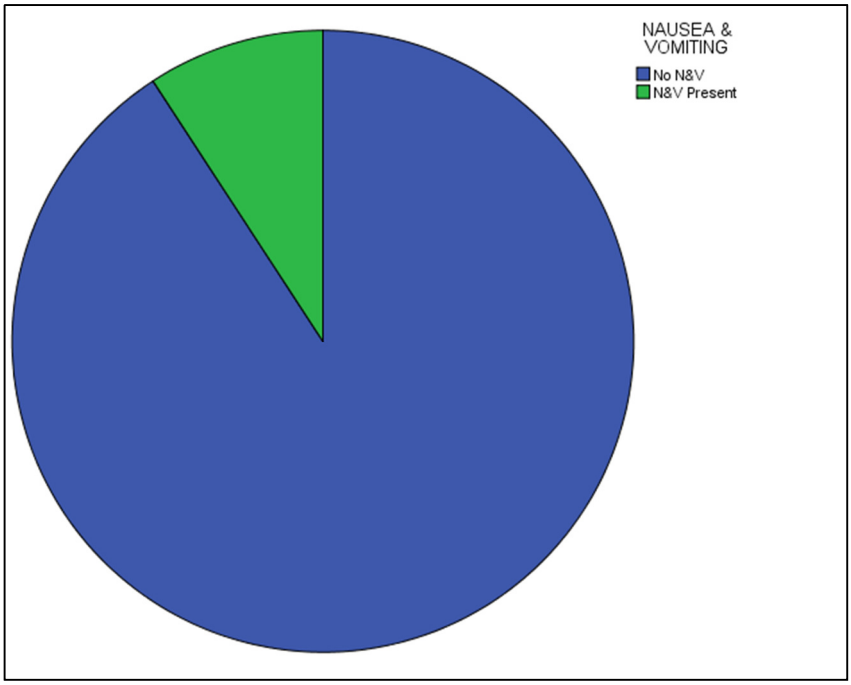


Figure 35: Pie chart showing number of patients with complaints of nausea and vomiting 30 min after initiation of HFNC therapy.

Table 28: Comfort level of the patient

PARAMETER		FREQUENCY	PERCENTAGE
COMFORT OF THE PATIENT	GOOD	35	46.1
	FAIR	34	44.7
	POOR	7	9.2

The above table shows that the comfort levels of 35 patients (46.1%) of the study population was good while 34 patients (44.7%) had a fair level of comfort only 7 patients (9.2%) were uncomfortable with HFNC therapy.

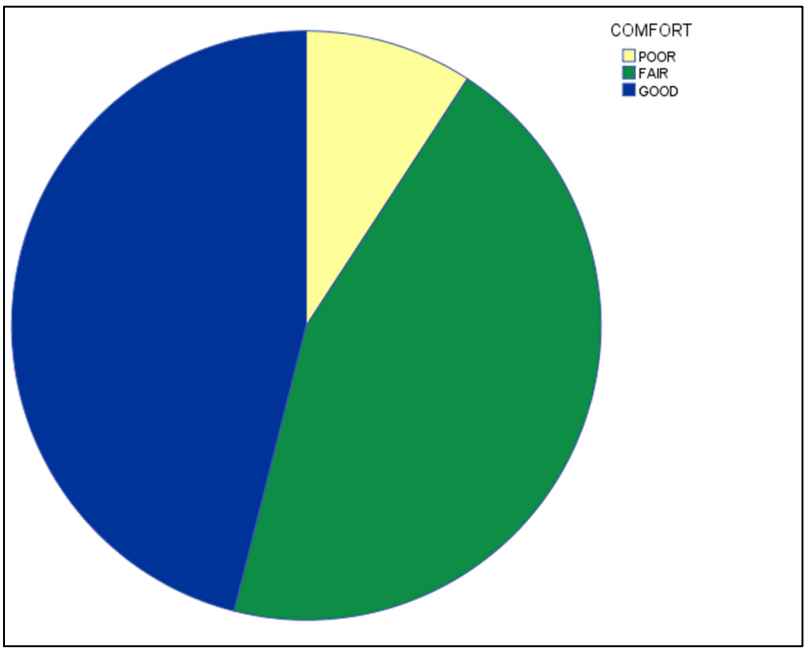


Figure 36: Pie chart showing number of patients with good, fair and poor comfort level 30 min after initiation of HFNC therapy.

Table 29: Total duration on HFNC (days) in the study population

PARAMETER		FREQUENCY	PERCENTAGE
TOTAL DURATION ON HFNC (days)	1-5	47	61
	6-10	21	27.6
	11-15	6	7.8
	16-20	2	2.6
	MEDIAN	4 (2.25, 8) (1-17)	

The above table shows that the median (IQR) (range) total duration on HFNC was 4 (2.25, 8) (1-17). Most of the patients (61%) were on HFNC for only 1-5 days.

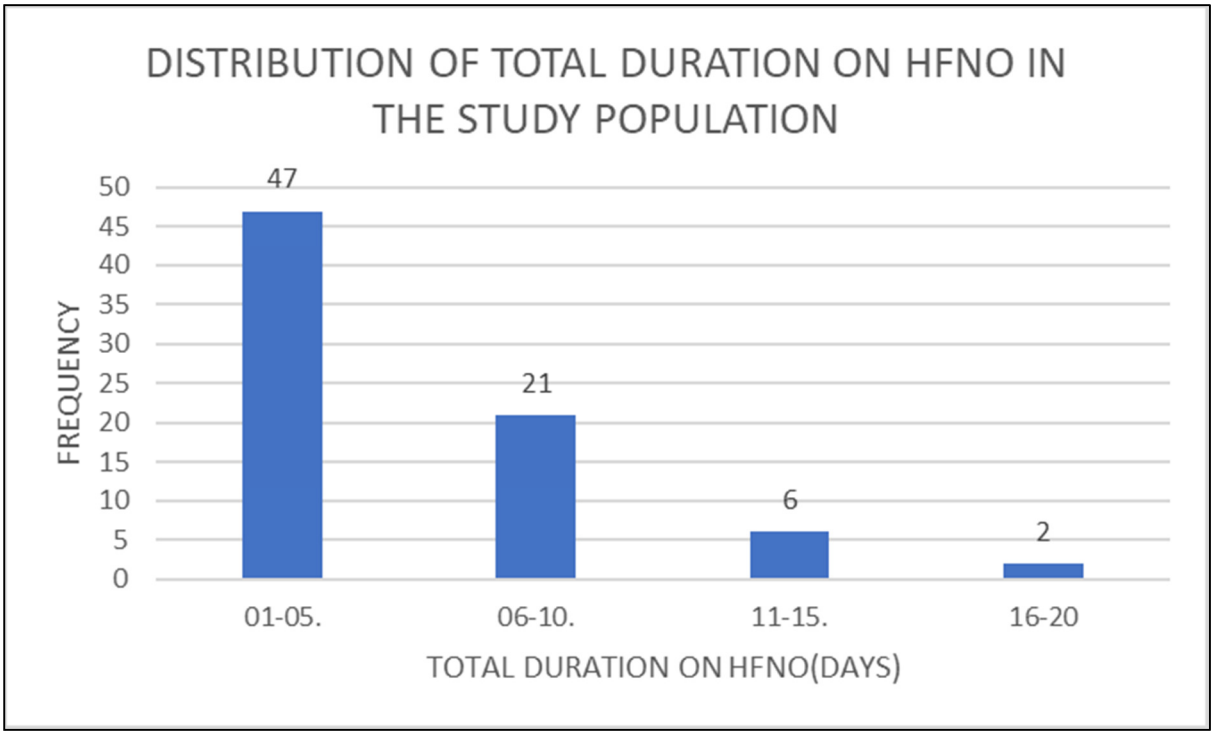


Figure 37: Bar chart showing total duration on HFNC in the study population

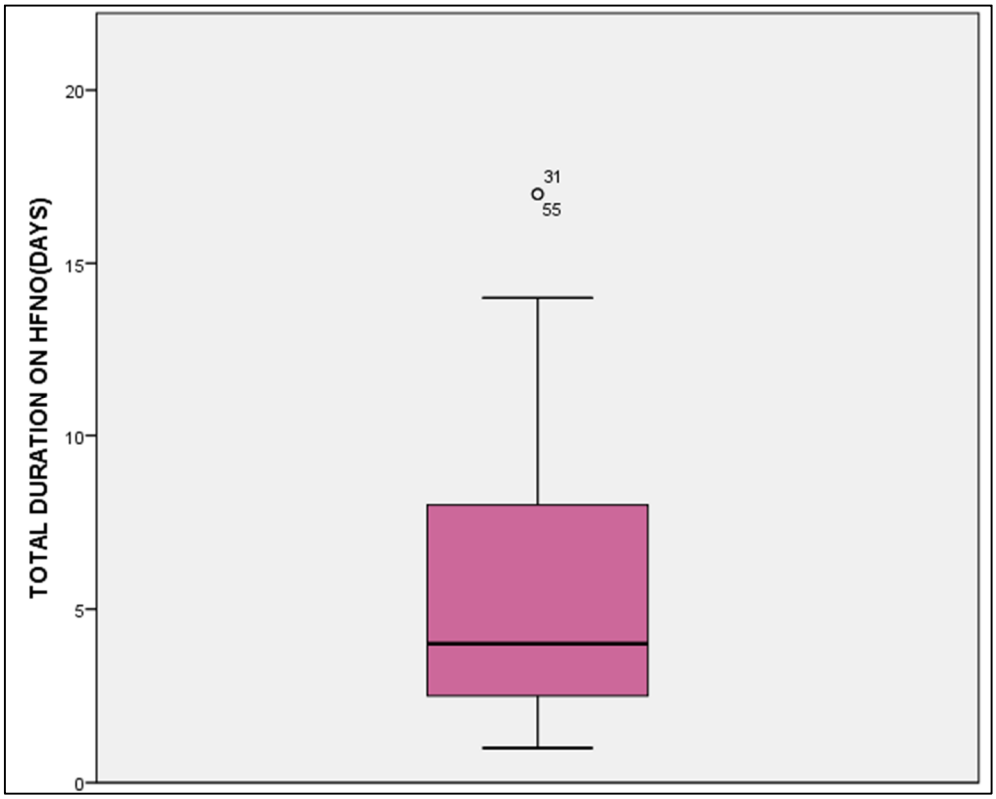


Figure 38: Box Plot showing median (IQR) (range) duration on HFNC therapy in the study population.

Table 30: Patient condition during HFNC therapy

PARAMETER		FREQUENCY	PERCENTAGE
PATIENT CONDITION DURING HFNO THERAPY	NOT IMPROVED	41	53.9
	IMPROVED	35	46.1

In our study population, out of 76 patients enrolled for the study, the condition of 46.1% (35) of the total patients improved and 53.9% (41) of the total patients worsened during HFNC therapy.

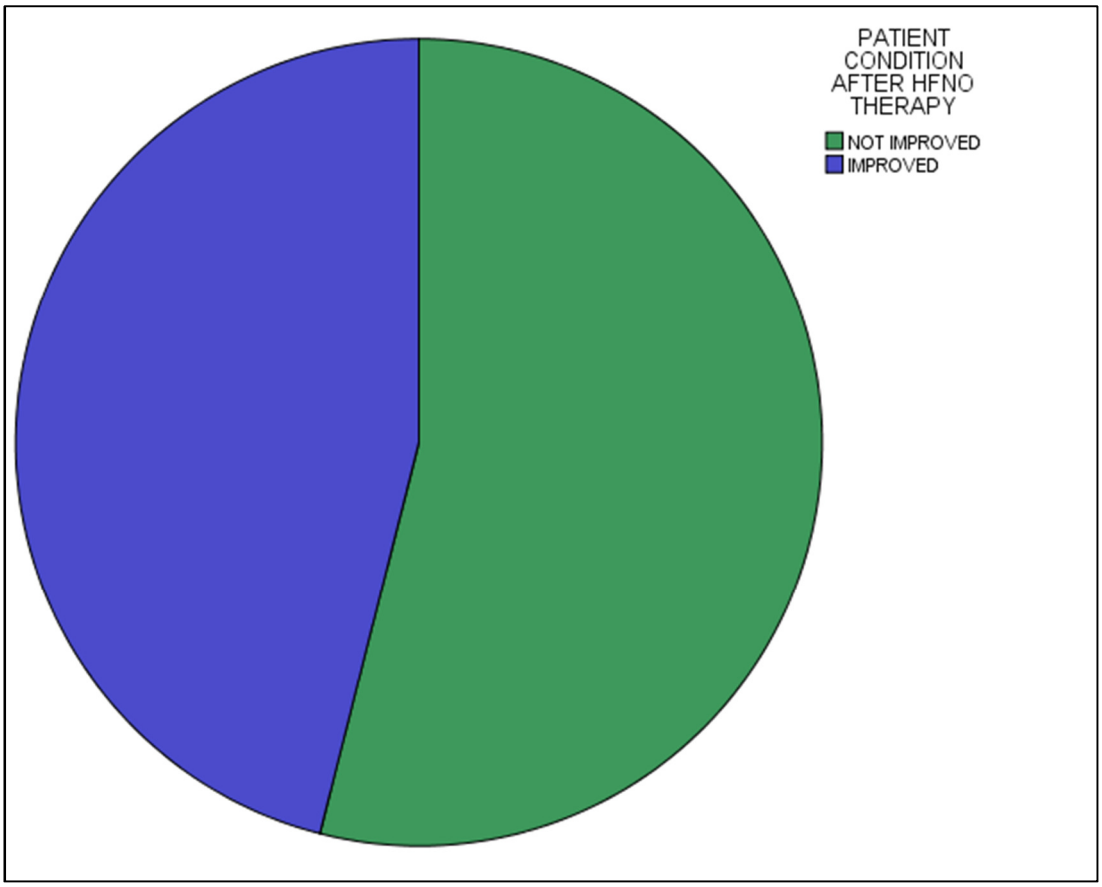


Figure 39: Pie chart showing number of patients' conditions during HFNC therapy.

Table 31: Subsequent therapy

PARAMETER		FREQUENCY	PERCENTAGE
SUBSEQUENT THERAPY	LOW FLOW OXYGEN THERAPY	35	46.1
	NIV	30	39.5
	INTUBATION	4	5.3
	DEATH	7	9.2

Out of 76 patients enrolled for the study, 35 patients (46.1%) were weaned off successfully from HFNC to Low flow oxygen therapy. 41 patients (53.9%) worsened in condition out of which 30 patients (39.5%) were subsequently treated with NIV, 5.3% of the patients were intubated and 7 patients (9.2%) succumbed to death.

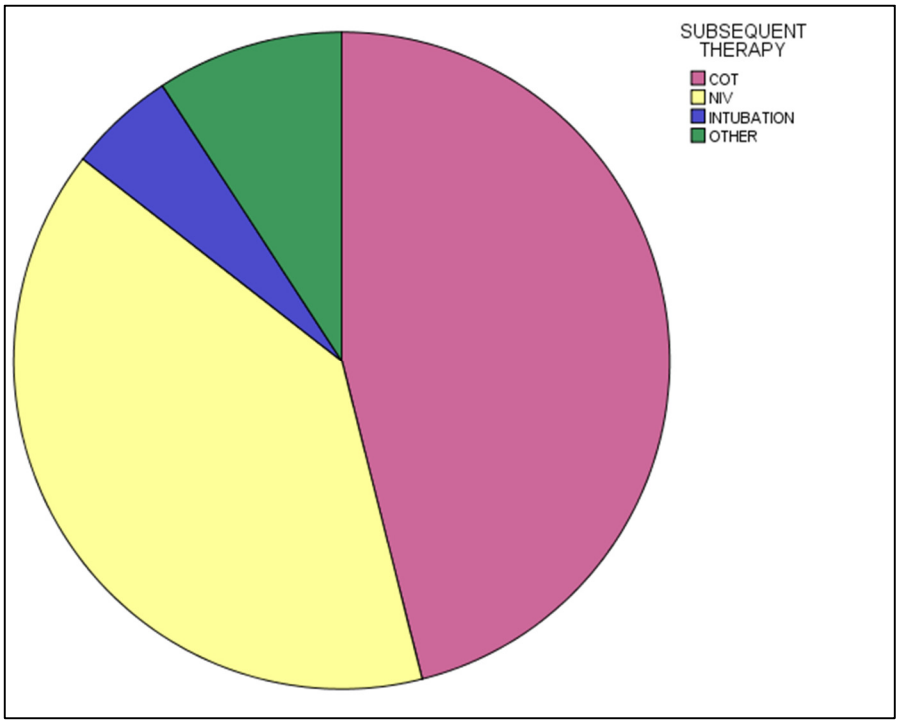


Figure 40: Pie chart showing subsequent therapy after HFNC therapy.

DISCUSSION

The use of HFNC in adult patients admitted in intensive care units could produce air leak in gastric antrum leading to gastric distention. The increase in the gastric volume can be attributed to both the increase in APD as well as increase in TVD after application of HFNC thereby increasing ACSA and GV. This increase in GV was associated with an increased number of peristaltic contractions and had a significant positive correlation with HFNC flow. Use of HFNC was associated with a significant increase in the SpO_2, PaO_2, PF-ratio and SaO_2 while a significant decrease was observed in the RR and $PaCO_2$. Most of the patients tolerated the HFNC therapy except for a few (complaining nausea and vomiting) and required the therapy for a period of 1-10 days. More than half of the patients improved on the therapy.

First line treatment for Acute Hypoxaemic Respiratory Failure is supplemental oxygenation. HFNC has recently become an alternative respiratory support that maintains adequate oxygenation and ventilate alveoli for critically ill patients. Many studies mention the ability of HFNC to decrease respiratory frequency, work of breathing and need for respiratory support escalation. Moreover, it delivers warm and adequately humidified gas and thus protects the mucociliary clearance mechanism of the patient. There are reports suggestive of a PEEP effect and an increased end-expiratory lung volume with usage of HFNC. Unlike NIV, HFNC cannot actively enhance tidal volume, but they help decrease the anatomic dead space as compared to other means.

Our study population of critically ill patients consisted of predominantly male gender (68.4%) having a median (IQR) (range) age (yrs) 61.5 (46.5, 68) (27-87), height (cm) 165 (159,168) (149-179), weight (kg) 68.5 (59,74) (45-90) and BMI (kg/m^2) 25.1 (22.9, 27.2) (16.3-31.2). Out of the total study population, 14.4% had DM only, 11.8% had DM and HTN, 9.2% had HTN only while 26.5% had other comorbidities. In our study population, with the help of ultrasonography, it was found that there was a significant increase in GV from baseline at 10 minutes, 20 minutes and 30 minutes after application of HFNC. The percentage of patients with gastric volume more than 0.8 ml/kg, considered as “at risk stomach” increased from 21% at 0 min to 59% at 30 min after application of HFNC.(19)

Elizabeth McLellan et al (2020) conducted a prospective, interventional assessor-blinded study in 60 subjects in healthy fasted adult volunteers and found that there was no evidence of gastric distension or an increase in gastric secretions with HFNC at flow rate up to 70 L/min for 30 min. (6) This study was conducted in healthy volunteers and hence the results obtained cannot be extrapolated to our study population which involves critically ill patients.

Satoki Inoue et al (2018) reported a case of a 21-month old boy with a history of chronic lung disease who was admitted in ICU with history of upper respiratory infection when taken on HFNC therapy post-extubation at 20L/min, developed severe stridor. A nasal airway was placed in the left nostril. Following this, the child developed signs of distress and critical abdominal distension which was later proven to be gastric insufflation. By this, they concluded that HFNC needs to be recognized as a positive pressure ventilation system and that critical over-distension of the abdomen can occur by HFNC (11). This case report goes in favour of our study results. But since the patient belongs to the paediatric age group and there was a history of deep placement of nasopharyngeal airway, it is difficult to expect these findings in the general population.

We have observed 14%, 52%, 59% incidence of "air leak" defined by qualitative ultrasound as a distended antrum with air content that blurs the posterior gastric wall at 10 min, 20 min and 30 min respectively after application of HFNC. The air leak was found to be present in significantly larger numbers of patients at 10 minutes (p value: 0.001), 20 minutes (p value: <0.0001), 30 minutes (p value: <0.0001) compared with baseline after application of HFNC. There was a significant increase in peristaltic contractions at 10 mins (<0.0001) after application of HFNC as compared to the baseline. The median difference in peristaltic contractions in the study population at 10 mins compared to baseline was 1 with a 95% confidence interval of -1.4 to -0.8. These observations helped in confirming our hypothesis. Sud et al done a blinded, non-randomised retrospective study and compared the gastric volumes acquired immediately after intubation measured by computed tomography in two series of adult patients, undergoing percutaneous thermal ablation of liver cancer under general anaesthesia: 50 received peri-intubation high flow nasal oxygen therapy and another 50 received conventional facemask pre-oxygenation and ventilation before intubation. There was a small amount of gas present in both the groups but no difference in the volume of gastric gas measured by computed tomography imaging between the two groups.(15) The use of general anaesthetic agents can increase the risk of aerophagia in these patients even with use of face mask ventilation. The time duration of use of HFNC in this study is shorter and hence the results cannot be equated with our study.

We have studied patients on different flows and on evaluation, there was a significant positive correlation between increase in flow and increase in gastric distention. Parke RL et al (2011) conducted a prospective descriptive study in patients who were scheduled for elective cardiac surgery in a tertiary care cardiothoracic and vascular ICU and measured

nasopharyngeal pressure with nasal flow oxygen at flows of 30, 40 and 50 L/min with patients mouth both open and closed. They concluded that mean nasopharyngeal pressure during nasal high flow oxygen increases as flow increases. (12) Lionel Bouvet et al (2014) conducted a prospective, randomized, double blind study in which 67 patients were allotted to 4 groups based on pressure applied during controlled pressure ventilation by face mask: 10, 15, 20 and 25 cmH2O after inducing patients with IV induction agents without muscle relaxation. There was a significant increase in incidences of gastric insufflation with inspiratory pressure from 0% in group P10 to 41% in group P25 according to auscultation and from 19 to 59% according to USG. Statistically significant increase in antral area was obtained in group P20 and P25 with insufficient lung ventilation in P10.(14).

These two studies throw light on the fact that increase in flows may increase nasopharyngeal pressures and this goes in support with our study as increase in pressures may ultimately lead to more aerophagia and gastric distention.

There was a significant increase in heart rate (p value< 0.0001) with a median difference of 0.5, significant increase in SPO_2 (p value< 0.0001) with a median difference of 5.5, significant decrease in RR (p value< 0.0001) with a median difference of 4 after 30 mins of application of HFNC. There was a non-significant change in SBP (p value= 0.429) DBP (p value= 0.376) MBP (p value= 0.974) at 30 mins compared to baseline on application of HFNC.

There was a significant increase in PaO_2 (p value= <0.0001) with a median difference of 6.9, significant increase in SaO_2 (p value< 0.0001) with a median difference of 3, significant decrease in $PaCO_2$ (p value<0.0001) with a median difference of 1.6, significant increase in PaO_2/FiO_2 (p value< 0.0001) with a median difference of 12.1 at 30 mins as compared to baseline.

Sztrymf B et al (2011) in his pilot prospective monocentric study in 38 patients evaluated safety and outcome of HFNC in ICU patients with Acute Respiratory Failure. It was found that HFNC significantly reduced RR, HR, dyspnoeic score, supraclavicular retraction and thoracoabdominal asynchrony and increased pulse oximetry as early as 15 minutes after beginning of HFNC. PaO2 and PaO2/FiO2 increased significantly after 1 hour of HFNC in comparison with baseline. (8).

These study results are consistent with our study results for RR, SPO_2, $PaO_2$and PaO_2/FiO_2values.The disparity in results for HR might be due to variation in illnesses of the

patient. Most of the patients enrolled in our study were covid positive patients and isolated. So, there is more risk of dehydration and anxiousness in these patients due to change in treatment modality

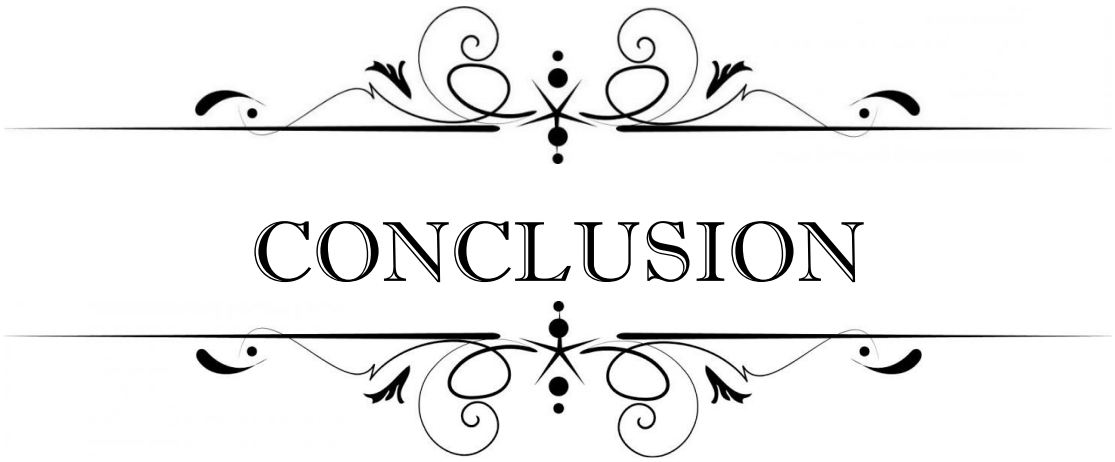
LIMITATION OF THE STUDY

There are several limitations to our study, which should be considered while interpreting our data. These are elucidated as follows:

1. It was an observational study, and not a randomized controlled trial, which is considered the gold standard.

2. A comparison of HFNC was not made with its peers - Non-invasive mechanical ventilation. Gastric insufflation is already a proven complication of non-invasive ventilation. A comparison between the two would have helped in establishing the severity of gastric distention with HFNC. Studies are warranted to compare the gastric distention following HFNC and NIV.

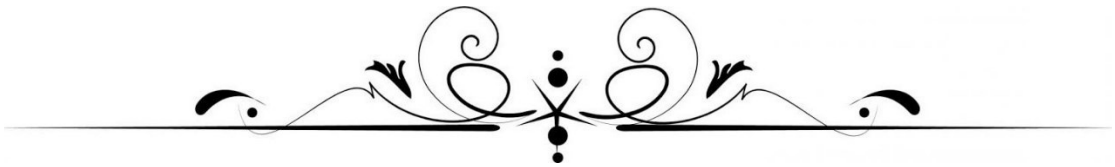
3. The data was only included for patients admitted between January 2021 and December 2021. This was because it was a time-bound study, with a schedule already decided in the protocol. There was an increased number of COVID admissions in this time period. So most of the cases that were included were critically ill patients due to SARS COV2 infection.



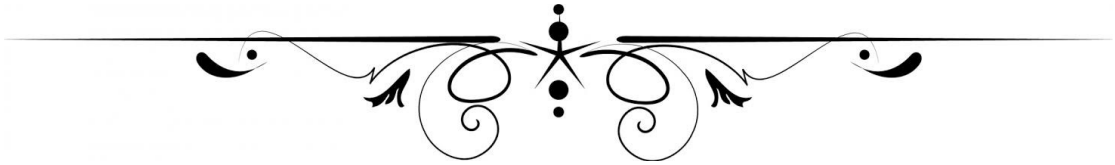
CONCLUSION

We had formulated a hypothesis that the use of HFNC in adult patients admitted in our intensive care unit could produce air leak in gastric antrum leading to gastric distention. The plausibility of this hypothesis was tested by a prospective observational study conducted in a timespan of one year from January 2021 to December 2021.The major findings of the study can be enlisted as below

1) The APD at 20 and 30 min were significantly larger compared to APD at 0 min while there was no significant difference between APD at 0 min and 10 min. The TVD, ACSA and GV at 10, 20 and 30 min were significantly larger compared to their measurements obtained at 0 min. The percentage of patients with gastric volume more than 0.8 ml/kg, considered as "at risk stomach" increased from 21% at 0 min to 59% at 30 min after application of HFNC. (19) Thus, we can conclude that the initiation of HFNC has significantly increased the gastric volume in critically ill patients.
2) There was a significant positive correlation (r=0.541) (p=<0.0001) between HFNC flow and increase in gastric volume.
3) Significantly higher numbers of patients had air leak at 10, 20 and 30 min compared with air leak at 0 min. The incidence of air leak at 10 minutes, 20 minutes and 30 minutes were calculated and found to be 14%, 52% and 59% respectively.
4) There was a significant increase in the number of peristaltic contractions at 10 mins after initiation of HFNC.
5) There was no significant change in HR, SBP, DBP and MBP from baseline noted at 30 min after initiation of HFNC. However, a significant increase in the SpO_2 and a significant decrease in the RR from baseline was observed at 30 mins after initiation of HFNC.
6) There was a significant increase in the PaO_2, PF-ratio and SaO_2 and a significant decrease in the $PaCO_2$ from baseline at 30 mins after application of HFNC.
7) Most of the patients tolerated the therapy while a few had nausea and vomiting. The duration of HFNC therapy for most of the patients was between 1 to 10 days and more than half of the patients improved with the therapy.



BIBLIOGRAPHY



1. Schwabbauer N, Berg B, Blumenstock G, Haap M, Hetzel J, Riessen R. Nasal high– flow oxygen therapy in patients with hypoxic respiratory failure: effect on functional and subjective respiratory parameters compared to conventional oxygen therapy and non-invasive ventilation (NIV). BMC anesthesiology. 2014 Dec;14(1):66.

2. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottereau A, Devaquet J. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. New England Journal of Medicine. 2015 Jun4;372(23):2185-96.

3. Maggiore SM, Idone FA, Vaschetto R, et al: Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. Am J Respir Crit Care Med 2014; 190: pp. 282-288

4. Itagaki T, Okuda N, Tsunano Y, et al: Effect of high-flow nasal cannula on thoracoabdominal synchrony in adult critically ill patients. Respir Care 2014; 59: pp. 70-74

5. De Keulenaer BL, De Backer A, Schepens DR, Daelemans R, Wilmer A, Malbrain ML. Abdominal compartment syndrome related to noninvasive ventilation. Intensive care medicine. 2003 Jul 1;29(7):1177-81.

6. McLellan E, Lam K, Behringer E, Chan V, Bozak D, Mitsakakis N et al. High-flow nasal oxygen does not increase the volume of gastric secretions during spontaneous ventilation. British J Anaesth. 2020; 125 (1): e75-e80

7. Inoue, Satoki et al. “A pediatric case developing critical abdominal distension caused by a combination of humidified high-flow nasal cannula oxygen therapy and nasal airway.” JA clinical reports vol. 4,1 (2018): 4. doi:10.1186/s40981-017-0143-

8. Lionel Bouvet, Marie-Laure Albert, Caroline Augris, Emmanuel Boselli, René Ecochard, Muriel Rabilloud, Dominique Chassard, Bernard Allaouchiche; Real-time detection of Gastric Insufflation Related to Facemask Pressure–controlled Ventilation Using Ultrasonography of the Antrum and Epigastric Auscultation in Nonparalyzed Patients:A prospective randomised double blind Study. Anesthesiology 2014;120(2):326-334..

9. Sud A, Athanassoglou V, Anderson EM, Scott S. A comparison of gastric gas volumes measured by computed tomography after high-flow nasal oxygen therapy or conventional facemask ventilation. Anaesthesia. 2021;76(9):1184-1189.

10. Perlas A, Chan VW, Lupu CM, Mitsakakis N, Hanbidge A. Ultrasound assessment of gastric content and volume. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2009 Jul 1;111(1):82-9.

11. Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D, Ricard JD. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive care medicine. 2011 Nov 1;37(11):1780.

12. Parke RL, McGuinness SP, Eccleston ML. A preliminary randomized controlled trial to assess effectiveness of nasal high-flow oxygen in intensive care patients. Respiratory Care. 2011 Mar 1;56(3):265-70.

13. Grieco DL, Menga LS, Raggi V, Bongiovanni F, Anzellotti GM, Tanzarella ES, Bocci MG, Mercurio G, Dell'Anna AM, Eleuteri D, Bello G. Physiological comparison of high-flow nasal cannula and helmet noninvasive ventilation in acute hypoxemic respiratory failure. American journal of respiratory and critical care medicine. 2020 Feb 1;201(3):303-12.

14. Vianello A, Arcaro G, Molena B, Turato C, Sukthi A, Guarnieri G, Lugato F, Senna G, Navalesi P. High-flow nasal cannula oxygen therapy to treat patients with hypoxemic acute respiratory failure consequent to SARS-CoV-2 infection. Thorax. 2020 Nov 1;75(11):998-1000.

15. Jaber S, Monnin M, Girard M, Conseil M, Cisse M, Carr J, Mahul M, Delay JM, Belafia F, Chanques G, Molinari N. Apnoeic oxygenation via high-flow nasal cannula oxygen combined with non-invasive ventilation preoxygenation for intubation in hypoxaemic patients in the intensive care unit: the single-centre, blinded, randomised controlled OPTINIV trial. Intensive care medicine. 2016 Dec;42(12):1877-87.

16. Di Mussi, Rosa et al. "High-flow nasal cannula oxygen therapy decreases post extubation neuroventilatory drive and work of breathing in patients with chronic obstructive pulmonary disease." Critical care (London, England) vol. 22,1 180. 2Aug. 2018, doi:10.1186/s13054-018-2107-9.

17. Parke RL, Eccleston ML, McGuinness SP. The effects of flow on airway pressure during nasal high-flow oxygen therapy. Respiratory care. 2011 Aug 1;56(8):1151-5.

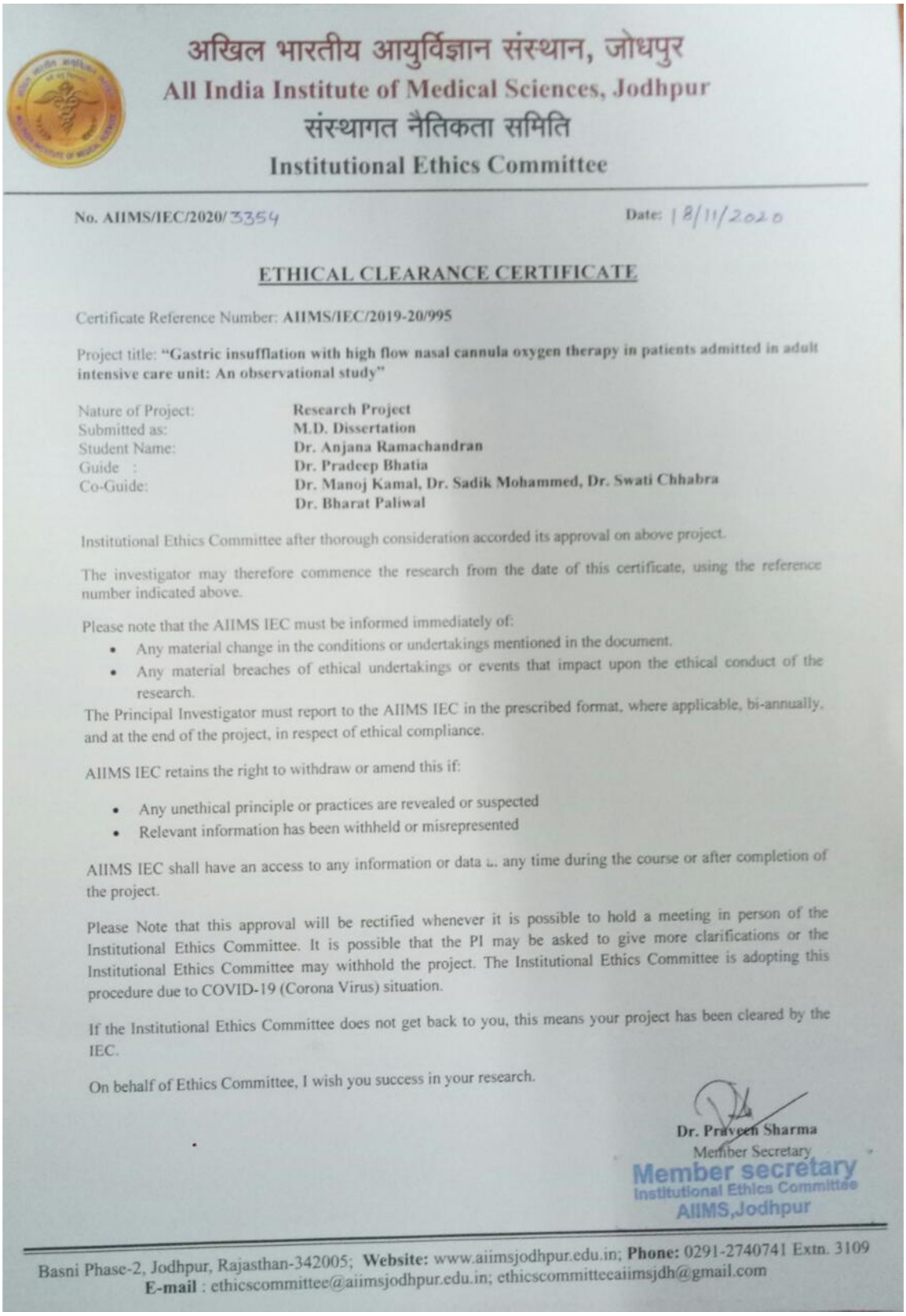
18. Inoue, Satoki et al. “A pediatric case developing critical abdominal distension caused by a combination of humidified high-flow nasal cannula oxygen therapy and nasal airway.” JA clinical reports vol. 4,1 (2018): 4. doi:10.1186/s40981-017-0143-

19. Hamada SR, Garcon P, Ronot M, Kerever S, Paugam-Burtz C, Mantz J. Ultrasound assessment of gastric volume in critically ill patients. Intensive care medicine. 2014 Jul 1;40(7):965-72.

ANNEXURES

ANNEXURE – 1

Ethical Clearance Certificate



अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/3354 Date: 18/11/2020

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2019-20/995**

Project title: **"Gastric insufflation with high flow nasal cannula oxygen therapy in patients admitted in adult intensive care unit: An observational study"**

Nature of Project:	**Research Project**
Submitted as:	**M.D. Dissertation**
Student Name:	**Dr. Anjana Ramachandran**
Guide :	**Dr. Pradeep Bhatia**
Co-Guide:	**Dr. Manoj Kamal, Dr. Sadik Mohammed, Dr. Swati Chhabra**
	Dr. Bharat Paliwal

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary
Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Basni Phase-2, Jodhpur, Rajasthan-342005; **Website:** www.aiimsjodhpur.edu.in; **Phone:** 0291-2740741 Extn. 3109
E-mail : ethicscommittee@aiimsjodhpur.edu.in; ethicscommitteeaiimsjdh@gmail.com

ANNEXURE - 2

All India Institute of Medical Sciences,

Jodhpur, Rajasthan

(Informed Consent Form)

TITLE: GASTRIC INSUFFLATION WITH HIGH FLOW NASAL CANNULA OXYGEN THERAPY IN PATIENTS ADMITTED IN ADULT INTENSIVE CARE UNIT: AN OBSERVATIONAL STUDY

Name of PG Student: Dr. ANJANA RAMACHANDRAN TelephoneNo:9961957533

Patient Identification No: _____

I,_____, s/o,d/o,r/o,_____

Resident of _____give my full, free, voluntary consent to be a part of the study“ Title: GASTRIC INSUFFLATION WITH HIGH FLOW NASAL CANNULA OXYGEN THERPY IN PATIENTS ADMITTED IN ADULT INTENSIVE CARE UNIT: AN OBSERVATIONAL STUDY” , the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions. I understand that my participation is voluntary, and I am aware of my right to opt out of the study at any time without giving any reason. I understand that the information collected and any of my medical records may be looked at by responsible individuals from AIIMS Jodhpur or from regulatory authorities. I give permission for these individuals to have access to my records.

Date: _____ _____

Place: _____ Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date : _____ _____

Place : _____ Signature of PG Student

Witness 1 Witness 2

_____ _____

Signature Signature

Name Name

ANNEXURE - 3

ऑल इंडिया इंस्टिट्यूट ऑफ मैडिकल साईडससं,

जोधपुर, राजस्थान

सूचित सहमचत प्रपत्र

थीडसस / डनबंध का शीर्षक: GASTRIC INSUFFLATION WITH HIGH FLOW NASAL CANNULA OXYGEN THERAPY IN PATIENTS ADMITTED IN ADULT INTENSIVE CARE UNIT: AN OBSERVATIONAL STUDY

पीजी छात्र का नाम: ि◌ॉं अंजना रामचन्द्रन टेल न: 9961957533

रोगी / स्वयंसेवक पहचान संख्या: _____

मैं, _____पुत्र / पुत्री _____

पता_____

अध्ययन GASTRIC INSUFFLATION WITH HIGH FLOW NASAL CANNULA OXYGEN THERAPY IN PATIENTS ADMITTED IN ADULT INTENSIVE CARE UNIT: AN OBSERVATIONAL STUDY

" का एक भाग बनने के डलए मेरी पूर्ष, स्वतंत्र, स्वैस्टिक सहमडत दें, डजसकी प्रडिया और प्रकृ डत मुझे अपनी पूरी संतुडि के डलए अपनी भार◌ा में समझाई गई है। मैं पुडि करता हं डक मुझे प्रश्न पूछने का अवसर डमला है। मैं समझता हं डक मेरी भागीदारी स्वैस्टिक है और मुझे डकसी भी कारर◌ड्डदए डबना डकसी भी समय अध्ययन से बाहर डनकलने के मेरे अडधकार की जानकारी है।

मैं समझता हं डक मेरे और मेरे मेडिकल ररकॉ◌िष के बारे में एकडत्रत की गई जानकारी को एम्स जोधपुर या डवडनयामक प्राडधकरर◌ो◌ं से डजम्मेदार व्यस्टि द्वारा देखा जा सकता है। मैं इन व्यस्टियों को अपने अडभलेखों तक पहंच के डलए अनुमडत देता हं।

तारीख: _____

_____

जगह: _____ हस्ताक्षर /

बाएं अंगूठे का छाप

यह प्रमाडर्त करने के डलए डक मेरी उपस्टस्थडत में उपरोि सहमडत प्राप्त की गई है।

तारीख: _____ _____

जगह: _____ पीजी छात्र के हस्ताक्षर

गवाह 1 गवाह 2

_____ _____

हस्ताक्षर हस्ताक्षर

नाम_____ नाम_____

पता_____ पता_____

ANNEXURE - 4

PATIENT INFORMATION SHEET

1. Risks to the patients: No interventions or life-threatening procedures will be done.
2. Confidentiality: Your participation will be kept confidential. Your medical records will be treated with confidentiality and will be revealed only to doctors/ scientists involved in this study. The results of this study may be published in a scientific journal, but you will not be identified by name.
3. Provision of free treatment for research related injury. Not applicable.
4. Compensation of subjects for disability or death resulting from such injury: Not Applicable
5. Freedom of individuals to participate and to withdraw from research at any time without penalty or loss of benefits to which the subject would otherwise be entitled.
6. You have complete freedom to participate and to withdraw from research at any time without penalty or loss of benefits to which you would otherwise be entitled.
7. Your participation in the study is optional and voluntary.
8. The copy of the results of the investigations performed will be provided to you for your record.
9. You can withdraw from the project at any time, and this will not affect your subsequent medical treatment or relationship with the treating physician.
10. Any additional expense for the project, other than your regular expenses, will not be charged from you.

ANNEXURE - 5

रोगी सूिना पत्रक

1. रोडगयों के डलए जोस्टखम: कोई हस्तक्षेप या जीवन-धमकी प्रडिया नहीं की जाएगी।

2. गोपनीयता: पकी भागीदारी को गोपनीय रखा जाएगा। पके मेडिकल ररकॉिष को गोपनीयता के साथ इलाज डकया जाएगा और के वल इस अध्ययन में शाडमल ि◌ॉक्टरों / वैज्ञाडनकों को पता चलेगा। इस अध्ययन के पररर◌ाम एक वैज्ञाडनक पडत्रका में प्रकाडशत हो सकते हैं, लेडकन पको नाम से पहचाना नहीं जाएगा।

3. अनुसंधान संबंधी चोट के डलए डन: शुल्क उपचार की व्यवस्था। लागू नही।ं

4. ऐसी चोट से उत्पन्न डवकलांगता या मृत्यु के डलए डवर्यों का मु वजा: लागू नहीं है

5. डकसी भी समय दंि या लाभों के नुकसान के डबना डकसी भी समय भाग लेने के डलए व्यस्टि को स्वतंत्रता लेने और अनुसंधान से वापस लेने के डलए स्वतंत्रता, डजसके तहत डवर्य अन्यथा हकदार होगा 6. पको जुमाषना या लाभ के नुकसान के डबना डकसी भी समय भाग लेने और अनुसंधान से वापस लेने की पूरी जादी है, डजस पर प अन्यथा हकदार होगं े।

7. अध्ययन में पकी भागीदारी वैकस्टिक और स्वैस्टिक है।

8. प्रदशषन की जांच की पररर◌ामों की प्रडत पके ररकॉिष के डलए पको उपलब्ध कराई जाएगी।

9. प डकसी भी समय पररयोजना से वापस ले सकते हैं, और यह पके बाद के डचडकत्सा उपचार या उपचार डचडकत्सक के साथ संबंध को प्रभाडवत नहीं करेगा।

9. पररयोजना के डलए कोई भी अडतररि व्यय, पके डनयडमत खचों के अलावा, पसे शुल्क नहीं डलया जाएगा।

ANNEXURE - 6

CASE RECORD FORM [A1]

PATIENT DETAILS

Name of the patient: Registration number

Age: Sex:

Height: Weight:

Diagnosis: Comorbidities

Duration of illness Medications

Time at which last feed taken by the patient

Time at which patient was started on HFNC therapy

FINAL OUTCOME

Total duration on HFNO :

Condition of the patient at the end of HFNO therapy: improved / not improved :

Subsequent therapy : Low flow oxygen therapy / NIV / Intubation /Other

Patient Sticker Here :

TABLE

Flow				
FiO_2				
	0 min	10 min	20min	30 min
Air Leak in gastrum				
No of peristaltic contractions in 1 min (At 0 min and 10 min)				
Anteroposterior diameter of antrum				
Transverse diameter of antrum				
Gastric volume				
HR				
BP				
SPO_2				
RR				

PaO_2				
$PaCO_2$				
PaO_2/FiO_2				
SaO_2				
Nausea and Vomiting				
comfort				