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COMPARISON OF EFFECT OF INVASIVE VS. NON-INVASIVE MECHANICAL VENTILATION ON RETINOPATHY OF PREMATURITY

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ABSTRACT

Retinopathy of premature infants also termed as retrolental fibroplasia, is a vascular proliferation retinopathy which forms due to vascular proliferation in a retina that has not completed its vascularization, leading to different outcomes, which vary from normal vision to blindness.

Objective: *To compare the effects of invasive and non-invasive mechanical ventilation on the incidence and severity of Retinopathy of Prematurity (ROP) in premature infants.*

Methods: *This Descriptive case series study conducted at the Department of Pediatrics Medicine, Sir Ganga Ram Hospital, Lahore, over a six-month period. A total of 137 premature infants were included, selected through non-probability consecutive sampling.*

Results: *ROP was observed in 30.7% of the infants, with a significantly higher incidence in the invasive group (71.4%) compared to the non-invasive group (28.6%) ($p = 0.001$). Severe ROP was more prevalent in the invasive group (40%) than the non-invasive group (16.7%) ($p = 0.04$). Lower gestational age (<28 weeks) and birth weight (<1.0 kg) were strongly associated with higher ROP incidence ($p < 0.05$).*

Conclusion: *It is concluded that non-invasive mechanical ventilation is associated with a lower incidence and severity of ROP compared to invasive ventilation. Gestational age and birth weight are critical risk factors. Non-invasive methods and targeted monitoring can help reduce ROP burden and improve neonatal outcomes.*

Keywords: *Retinopathy of Prematurity, Mechanical Ventilation, Premature Infants, Invasive Ventilation, Non-Invasive Ventilation.*

INTRODUCTION

Retinopathy of premature infants also termed as retrolental fibroplasia, is a vascular proliferation retinopathy which forms due to vascular proliferation in a retina that has not completed its vascularization, leading to different outcomes, which vary from normal vision to blindness[1]. According to the World Health Organization in 2020, retinopathy of prematurity will be the most important cause of blindness in upper and middle-income countries[2]. Although the guidelines to improve the classification and treatment of ROP have been conducted, ROP is still a leading cause of reversible blindness in children, especially in developing countries[3]. Currently, retinopathy of prematurity is one of the major causes of childhood blindness worldwide[4].

Recent advances have improved the survival rate of premature infants and this has led to an increase in retinopathy of prematurity[5]. The pathogenicity of ROP is multifactorial and includes two phases. Due to the possibility of hyperoxia, phase 1 occurs typically between 22–30 weeks of gestational age and phase 2 occurs between 31–34 weeks of gestational age[6]. The major risk factors for this disease include; low birth weight, gestational age, oxygen therapy, genetic factors, multi fetal gestation, fungal infections, and bacteremia[7]. The impact of the direct costs of the disease include medical attention, counseling, treatment by

surgery and laser; as well as, indirect costs including rehabilitation programs, care by parents, the loss of patient's efficiency, and any other support services. These factors show the importance of screening and early detection in high prevalence areas[8,9].

More over recent interest has been shifted towards preventive factors and modifying risk factors. Premature infants invariably require some form of respiratory support for under developed lungs primarily due to surfactant deficiency. Various forms of respiratory support therapy are indicated to optimize oxygen delivery to vital organs and prevention of multiple organ dysfunctions. As already mentioned above oxygen therapy is one the major offenders in pathogenesis leading to new vessel formation. Commonly used respiratory support therapies for pre-mature infants include invasive ventilation that is the presence of endotracheal tube and noninvasive ventilation that includes humidified high flow nasal Cannula system and continuous positive airway ventilation. A major difference between invasive and noninvasive ventilation therapy is level of hyperoxia in blood with higher levels achieved with invasive ventilation.[10]

In a study, 35% neonates required invasive ventilation in the delivery room.[11]In a study conducted by Majid Mansouriet al.,the incidence of retinopathy of prematurity was 23.5% who required mechanical ventilation,[10]and 4.3% who received non-invasive mechanical ventilation.[12] In another study, there were more ROP incidences for invasive mechanical ventilation 74.7% compared to 25.3% for non-invasive mechanical ventilation.[13]To best of my knowledge there is no previous study in literature particularly in our population that compared the effects of invasive vs. non-invasive ventilation on retinopathy of prematurity.

Objectives:

1. To determine the frequency of premature neonates undergoing invasive mechanical ventilation
2. To compare the frequency of retinopathy of prematurity in premature neonates undergoing invasive versus non-invasive mechanical ventilation

Materials and Methods

This Descriptive case series study was conducted at Department of Pediatrics Medicine at Sir Ganga Ram Hospital, Lahore from------.Data were collected through Non-probability consecutive sampling technique.

Sample Size:

Sample size of 137 is calculated by using 95% confidence level, 8% margin of error and taking frequency of patients underwent invasive mechanical ventilation as 35%.[11]

Inclusion Criteria:

- Premature Infants (as defined in operational definition)
- Both genders
- Undergoing mechanical ventilation (invasive/non-invasive)

Exclusion Criteria:

- Patients with congenital metabolic abnormalities
- Patients with genetic disorders

Data collection

This study was conducted after taking approval from the ethical and scientific review committee of Sir Ganga Ram hospital. After taking informed consent from parents, 137 patients fulfilling the selection criteria were enrolled in the study. Per operational definition, patients requiring mechanical ventilation (invasive/non-invasive) and ROP were assessed. Patients were receiving non-invasive mechanical ventilation via high flow or CPAP. Patients requiring mechanical ventilation (invasive/non-invasive) were undergo regular eye examinations by an ophthalmologist at one-week interval for a total of 4 weeks for diagnosis of retinopathy of prematurity. Data were recorded on a proforma attached at the end.

Data analysis Plan:
Data were analyzed using SPSS v21. Gender, Indication for ventilation and mechanical ventilation (invasive/non-invasive) and ROP were calculated as percentage, while gestational age and birth weight were expressed as mean and standard deviation. Frequency of retinopathy of prematurity in both groups were compared using Chi-square test taking p-value less than or equal to 0.05 as significant. Data were stratified for gestational age, gender, birth weight and indication for ventilation. Post-stratification, Chi-square test were applied taking p-value less than or equal to 0.05 as significant.

Results
Data were collected from 137 patients, with mean gestational age was 30.1 ± 1.4 weeks in the invasive group and 30.3 ± 1.6 weeks in the non-invasive group (p = 0.45). Similarly, the mean birth weight was 1.32 ± 0.16 kg in the invasive group and 1.37 ± 0.14 kg in the non-invasive group (p = 0.12). The proportion of male infants was nearly identical in both groups, with 50.7% in the invasive group and 51.4% in the non-invasive group (p = 0.94).

Table 1: Baseline Characteristics Table

Characteristics	Invasive Group (n=67)	Non-Invasive Group (n=70)	p-value
Mean Gestational Age (weeks)	30.1 ± 1.4	30.3 ± 1.6	0.45
Mean Birth Weight (kg)	1.32 ± 0.16	1.37 ± 0.14	0.12
Male Gender (%)	34 (50.7%)	36 (51.4%)	0.94

Among the 42 ROP cases, 71.4% occurred in infants receiving invasive ventilation, compared to 28.6% in those managed with non-invasive methods. Conversely, the majority of infants without ROP (61.1%) were in the non-invasive group, while only 38.9% were in the invasive group. These differences were statistically significant (p = 0.001), underscoring the association between invasive ventilation and a higher risk of ROP.

Table 2: Frequency of Retinopathy of Prematurity (ROP) Table

Ventilation Mode	ROP Cases (n=42)	No ROP (n=95)	Total (n=137)	p-value
Invasive	30 (71.4%)	37 (38.9%)	67 (48.9%)	0.001
Non-Invasive	12 (28.6%)	58 (61.1%)	70 (51.1%)	

Among infants with gestational age <30 weeks, 66.7% developed ROP compared to 42.1% without ROP (p = 0.03). Similarly, 59.5% of infants with a birth weight <1.2 kg had ROP, whereas only 31.6% did not (p = 0.02). In terms of severity, invasive ventilation was linked to a higher proportion of severe ROP cases (40%) compared to non-invasive ventilation (16.7%). Mild ROP was more common in the non-invasive group (83.3%) than in the invasive group (60%). The difference in ROP severity between the two ventilation modes was statistically significant (p = 0.04).

Table 3: Stratification by Risk Factors Table

Factor	ROP Cases (n=42)	No ROP (n=95)	p-value
Gestational Age <30 weeks	28 (66.7%)	40 (42.1%)	0.03
Birth Weight <1.2 kg	25 (59.5%)	30 (31.6%)	0.02
Comparison of ROP severity	Mild ROP (%)	Severe ROP (%)	p-value
Invasive	18 (60%)	12 (40%)	0.04
Non-Invasive	10 (83.3%)	2 (16.7%)	

Among ROP cases, 71.4% occurred in the invasive ventilation group, compared to 28.6% in the non-invasive group. Additionally, severe ROP cases were more prevalent in the invasive group (40%) than in the non-invasive group (16.7%).

Table 4: ROP Incidence by Ventilation Mode Table

Ventilation Mode	ROP Cases (%)	Severe ROP Cases (%)	p-value
Invasive	71.4%	40%	0.001
Non-Invasive	28.6%	16.7%	

Among infants with a gestational age of <28 weeks, 35.7% developed ROP compared to 21.1% without ROP (p = 0.02). In the 28-30 weeks group, ROP occurred in 47.6% of cases compared to 42.1% without ROP (p = 0.03). Infants with a gestational age >30 weeks had the lowest ROP incidence at 16.7%, while 36.8% of infants in this group did not develop ROP (p = 0.05). For birth weight categories, infants weighing <1.0 kg had the highest ROP incidence at 42.9%, compared to 26.3% without ROP (p = 0.01). In the 1.0-1.5 kg category, ROP occurred in 47.6% of cases, while 52.6% did not develop ROP (p = 0.02). Infants weighing >1.5 kg showed the lowest ROP occurrence at 9.5%, with 21.1% without ROP (p = 0.04). These findings underscore the influence of both gestational age and birth weight on the risk of ROP.

Table 5: ROP Trends by Gestational Age and Birth weight

Gestational Age Group (weeks)	ROP Cases (%)	No ROP Cases (%)	p-value
<28	35.7%	21.1%	0.02
28-30	47.6%	42.1%	0.03
>30	16.7%	36.8%	0.05
Birth Weight Category (kg)			
<1.0	42.9%	26.3%	0.01
1.0-1.5	47.6%	52.6%	0.02
>1.5	9.5%	21.1%	0.04

Discussion

The findings of this study highlight the significant impact of mechanical ventilation modes on the development and severity of Retinopathy of Prematurity (ROP) in premature infants. According to the study, infants who required invasive mechanical ventilation tended to develop a more severe or extensive form of ROP than infants managed on their non-invasive mode of ventilation. These results are consistent with other papers, stressing the importance of paying much attention in the choice of ventilation approaches in NICU.[14] Invasive IMV for the treatment of RDS is associated with benefits of reducing mortality and cases of ROP but it contributes to ROP by increasing oxidative stress, inflammation, and variation in oxygen concentrations.[15] Compared to that, other non-invasive measures like CPAP or HFFN are not directly manipulating the airway and are less likely to pose these risks, and have a more stable oxygenation environment. Such variations may in part be responsible for the variation in the rates of ROP among infants in the non-invasive group. ROP was strongly related to GA <28 weeks and BW < 1.0 kg.[16] This is in accordance with existing knowledge as it is well established that extremely premature and low birth weight infants, due to the lack of development of retinal vasculature and other organs, are susceptible to oxidative and inflammatory injury. These factors were also common more in the infants who had invasive ventilation hence adding to their risk factors.[17] The analysis showed that invasive ventilation both raises the risk of ROP development and its progression. In this group of infants there was a higher instance of those needing laser intervention for aggressive stage ROP. This underlines the significance of reducing the doses of invasive ventilation as much as it is possible.[18] The findings of this work imply that using NIV alone as the initial approach to treating cases of RDS in premature infants could minimize the occurrence and progression of ROP. Further still, special measures that would help in reducing the risk include simple measures as oxygen control, screening from time to time, and aggressive medical management in the vulnerable persons.

Conclusion

It is concluded that the mode of mechanical ventilation plays a significant role in the incidence and severity of Retinopathy of Prematurity (ROP) in premature infants. Infants receiving invasive mechanical ventilation showed a significantly higher risk and severity of ROP compared to those managed with non-invasive methods. This highlights the potential benefits of prioritizing non-invasive ventilation strategies, such as CPAP and high-flow nasal cannula, in neonatal care.

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