International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 10, 2020
ISSN: 1475-7192

Impact ofTotal Parenteral nutritionon Outcomes of Neonatal Intensive Care Units

[1]EhabAbdelmonem El-banna, [2]HebaGamalAnany, [3]Aya Ismail Kotb Mohamed

Abstract

Background:*Total Parenteral nutrition (TPN) can be life saving for neonates who cannot receive adequate enteral nutrition because of inability to tolerate enteral feeds.The ASPEN's standards of practice participate in the development, implementation and has provided excellent guidelines to address each of the components of TPN. The objectives of this work were to determine the outcomes of neonates on total parenteral nutrition prepared without laminar (retrograde) or prepared with laminar unit.****Methods:****This retrospective prospective cohort study included 420 neonates, the without laminar group cases where TPN is prepared on ward include (150) and the laminar group cases where TPN prepared is on TPN unit using laminar flow include (270).All neonates in our study were subjected to full history taking, clinical examination, laboratory investigations on admission and on discharge and the protocol of treatment according to unit protocol****. Results:****There is significant difference between 2 groups as regard presence of maternal history and as regard PROM.There is high significant difference between 2 groups as regard Hb, CRP, and Ca level on discharge there is increase in the laminar group.There is high significant difference between 2 groups as regard short term outcome, neurodevelopmental delay and as regard bronchopulmonary dysplasia.There is high significant difference between 2 groups as regard Develop sepsis and as regard weight on discharge.*

Conclusion: *Using laminar flow in TPN preparation decrease mortality rate ,occurrence of neurodevelopmental delay ,bronchopulmonary dysplasia.*

Key words: *outcomes - neonates -total parenteral nutrition- without laminar- laminar unit*

I. Introduction:

Parenteral nutrition (PN) is the feeding of special nutritional products to the neonates intravenously, to bypassing the usual process of eating and digestion. The products are made by specialist pharmaceutical compounding companies and are considered to be the highest risk pharmaceutical preparations available as the products cannot undergo any form of terminal sterilization.The neonate takes highly complex nutritional formulae that contain nutrients such as glucose, salts, amino acids, lipids and added vitamins and dietary minerals. It is called total parenteral nutrition (TPN) or total nutrient admixture (TNA) when no significant nutrition is obtained by other routes, and partial parenteralnutrition (PPN) when nutrition is also partially enteric.

[1] *Professor of pediatrics, Faculty of Medicine – Zagazig University.*
[2] *Assistant professor of pediatrics, Faculty of Medicine – Zagazig University*
[3] *M.B.B.CH 2012, Zagazig University*

It may be called peripheral parenteral nutrition (PPN) when administered through vein access in a limb rather than through a central vein as central venous nutrition (CVN**).** [**1**]

TPN may be short-term or long-term nutritional therapy, and may be administered on acute medical floors as well as in critical care areas. The caloric requirements of each patient are individualized according to the degree of stress, organ failure, and percentage of ideal body weight. TPN is used with patients who cannot orally ingest or digest nutrition [**2**]**.**

Preterm infants in a neonatal intensive care unit are completely dependent on total parenteral nutrition (TPN) for adequate food intake until enteral feeding in sufficient amounts is well tolerated**.** [**3**]

Parenteral nutrition is the only way to provide the necessary nutrients for days or weeks. as parenteral nutrition is not a "natural" way of feeding but an invasive procedure, it also carries potential risks. Therefore, it is important to only use parenteral nutrition when indicated and to always try tosupport enteral nutrition if possible [**4**]**.**

Standardized parenteral nutrition solutions are generally preferred over individualized parenteral nutrition solutions as they safely meet the needs of the majority of infants. [**5**]

PN is usually prepared at hospital pharmacies as a 'centralized preparation', but at some hospitals still prepared on ward by nurses. an European survey performed in 2010 by [**6**]showed that 12% of PN are prepared on hospital wards. The requirements for the preparation area, the personnel's training and the quality control regarding intravenous medication preparation including PN vary greatly**.** [**7**]

Hospital pharmacies mostly follow the current 'EU guidelines to Good Manufacturing Practice' (GMP) byand are obliged to apply the guidelines of the 'Pharmaceutical Inspection Convention/ Pharmaceutical Inspection Co-Operation Scheme' (PIC/S) for health system establishments, so they must produce in laminar airflow hoods in clean rooms with validated operators. Hospital wards do not need to follow these guidelines. They are not always in possession of laminar airflow hoods to assure a clean preparation and they are not equipped and trained to realise quality controls**.** [**8**]

The study aimed tocompare the impact of TPN between neonates that received TPN prepared with the laminar flow with the neonates received TPN prepared without laminar flow in Neonatal Intensive Care Units of Zagazig University Children's Hospital.

II. Patients and Methods

Our retro and prospective cohort study was carried out in Neonatal Intensive Care Unit in Zagazig University Children's Hospital. All experimental procedures were approved and formed in accordance with the guidelines of Institutional Review Board (IRB) of Faculty of Medicine, Zagazig University, Egypt (Approval No.: ZU-IRB #5712/25-11-2019

The total sample size is 420 neonates divided into two groups:

- **First Group:** (cases received total parenteral nutrition prepared with lminar flow):

This group included 270 neonates admitted to neonatal intensive care unit (NICU) needing TPN ,147(54,4%)were malesand 123(45.6%) were females and there gestational age ranged from 26-42 weeks.

- **Second Group:**(cases received totalparenteral nutrition prepared without laminar):

This group included 150 neonates admitted to neonatal intensive care unit (Nicu)in the past time (archived cases) need TPN ,91(60,7%) were malesand 59 (39,3%) were females and there gestational age ranged from 26-42 weeks.

Target population:

Neonates were selected to participate in the study on the basis of according to the following inclusion and exclusion criteria:

Inclusion criteria: Age from (0-28) day. Cases on total parenteral nutrition admitted to Neonatal Intensive Care Unit in Zagazig University Children's Hospital.Gestational age from (26-42)week.

Exclusion criteria: Ageabove one month**.** Neonates diagnosed with genetic defects by coarse features.Neonates diagnosed with malignancy.

Duration of the study : 6 months

Methods:

Full History Taking:

- Prenatal history including gestational age (full term –preterm), maternal history including any chronic maternal diseaseand medical history, Rh, blood group, family history and treatment protocol during pregnancy.
- Natal history including mode of delivery and obstetrical history.
- Postnatal history including birth weight, appearance, color, activity and presenting symptoms.

Physical examination:

- Generalexamination.
- Abdominal examination.
- Chest examination
- Cardiac examination.
- Adequate Neurological examination and Follow up of the laminar group for six month and the group without laminar by good history taking for detection of any neurodevelopmental delay with special focus on:

- **Motor milestone:** By three months your baby can control his head when he's being supported to sit. By six months, he will have neck muscles that are strong enough to hold his head up and turn it from side to side.[**9**]**(De Sanctis et al., 2016).**
- **Mental milestone:** between 6 and 8 weeks of life, babies develop a "social smile" an intentional signal of warmth just for you. This is an important milestone. [**10**](**Voytas, 2018).**

- **Examination of neonatal sepsis by:**

- **Clinical variables**

1) Temperature instability
2) Heart rate _180 beats/min or _100 beats/min
3) Respiratory rate >60 breaths/min plus grunting or desaturations
4) Lethargy/altered mental status
5) Glucose intolerance (plasma glucose >10 mmol/l)
6) Feed intolerance.

- Assessment of prescription, preparation, administration and follow-up of the TPN with special attention to the gastrointestinal tract, liver and nutritional status according to the guidelines of The European Society for Paediatric Gastroenterology Hepatology and Nutrition [**11**] **(Riskin et al., 2006).**

- Assessment of gestational age by The New Ballard score (NBS)[**12**] **(Ballard, et al., 1991).**

- the most widely used method in assessment of gestational age is the Ballard Score, a manual scoring system that looks at neuromuscular and physical attributes of newborns [**13**](**Torres et al., 2017).**

Laboratory Investigations:

Essential investigations for all cases included:

- Liver functions.
- Serum electrolyte levels.
- Blood glucose level daily.
- Inflammatory variables for detection of sepsis including:

1) Leukocytosis (WBC count >34 000_109/l)
2) Leukopenia (WBC count <5000_109/l)
3) Immature neutrophils >10%
4) Immature:Total neutrophil ratio >0.2
5) Thrombocytopenia <100 000_109/l
6) CRP >10 mg/l or 2 SD above normal value

- Lipid profile.
- blood culture:

Blood culture remains the gold standard for the management of neonatal sepsis. Blood Culture reports aids physician in either optimizing therapy or timely discontinuation of antibiotics. [**14**](**Guerti et al., 2011).**

- Computed tomography (CT): for some cases like cases with convulsion and increased head circumference.
- CSF:for diagnosis of meningitis if indicated as in neonatal bacterial meningitis there is higher CSF WBC counts, higher CSF protein concentrations, and lower CSF glucose concentrations. [**15**](**Thomson et al., 2018)**.

STATISTICAL ANALYSIS

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. The used tests were : Chi-square test:Fisher's Exact or Monte Carlo correction: Student t-test: Mann Whitney test[**16**](**Albers, 2017)**

III. Results:

This table shows that there were 270 (64.3%) with laminar, 150 (35.7%) without laminar.**Table (1)**

There is highly significant decrease in weight of admission in the group with laminar. **Table (2)**There is significant increase in the maternal problems during pregnancy in the laminar group especially premature rupture of membrane**Table (3)**.

There is highly significant increase in Hb level in the laminar group **Table (4)**.

There is significant increase in Ca++ level in group with laminar **Table (5)**.

There is significant increase in albumin level and significant improvement in liver functions in the laminar group **Table (6)**

There is increase in percent of negative blood culture in laminar group but without significant value.

The most common organism is klebsiella and the most sensitive antibiotic is tygacil in both groups.**Table (7)**

There is highly significant decrease in percent of sepsis and increase in weight of discharge in laminar group. **Table (8)**

There is highly significant decrease in occurance of neuro developmental delay and bronchopulmonary dysplasia in laminar group. **Table (9)**

Table (1): Distribution of the studied cases according to laminar or without laminar.

Laminar or without laminar	No.	%
Laminar	270	64.3
Without laminar	150	35.7

Table (2): Comparison between the two studied groups according to demographic data.

Demographic data	Without laminar (n = 150)		With laminar (n = 270)		Test of Sig.	P
	No.	%	No.	%		
Sex						
Male	91	60.7	147	54.4	χ^2= 1.520	0.218
Female	59	39.3	123	45.6		
Mode of Delivery					0.559	0.455
NVD	37	24.7	58	21.5		
C.S	113	75.3	212	78.5		
Gestational age (weeks)						
Min. – Max.	26.0 – 42.0		26.0 – 42.0		t= 0.665	0.507
Mean ± SD.	36.63 ± 4.07		36.37 ± 3.71			
Median (IQR)	37.0 (36.0 – 40.0)		37.0 (35.0 – 40.0)			
Weight of admission (kg)						
Min. – Max.	0.80 – 4.0		0.80 – 4.0		U= 871.50*	<0.001*
Mean ± SD.	3.03 ± 0.68		2.31 ± 0.79			

Median (IQR)	3.0 (2.70 – 3.60)	2.40 (1.60 – 2.90)		
Age (days)				
Min. – Max.	1.0 –38.0	1.0 – 40.0	t= 0.561	0.575
Mean ± SD.	25.93 ± 6.97	25.46 ± 8.85		
Median (IQR)	25.0 (20.75 – 31.25)	24.0 (18.0 – 34.0)		

t: Student t-testU: Mann Whitney test χ^2: **Chi square test**

p: p value for comparing between the two studied groups NVD/normal vaginal delivery

*: Statistically significant at $p \leq 0.05$ C.S/cesarean section

Group A: Archive group

Group B: New group

Table (3): Comparison between the two studied groups according to maternal history.

Maternal history	**Without laminar (n = 150)**		**With laminar (n = 270)**		χ^2	**P**
	No.	**%**	**No.**	**%**		
No maternal problem	130	86.7	211	78.1	4.582*	0.032*
Yes (with maternal problem)	**20**	**13.3**	**59**	**21.9**		
DM	7	35.0	14	23.8	0.972	FEp=0.324
Anhydraminous	1	5.0	1	1.7	0.179	FEp=1.000
RH negative mother	2	10.0	4	6.8	0.015	FEp=1.000
HTN	0	0.0	3	5.1	1.679	FEp=0.556
Cardiomyopathy	2	10.0	3	5.1	1.424	FEp=0.254
Placenta previa	2	10.0	4	6.8	0.015	FEp=1.000
Pre eclampsia	2	10.0	3	5.1	1.424	FEp=0.254

Oligohydraminous	1	5.0	3	5.1	0.040	^{FE}p=1.000
UTI	0	0.0	3	5.1	1.679	^{FE}p=0.556
Polyhydraminos	1	5.0	3	5.1	0.040	^{FE}p=1.000
PROM	0	0.0	10	16.9	5.691*	^{FE}p=0.016*
Eclampsia	0	0.0	2	3.4	1.116	^{FE}p=0.540
Vaginal. Bleeding	2	10.0	4	6.8	0.015	^{FE}p=1.000
Anemia	0	0.0	2	3.4	1.116	^{FE}p=0.540

FE**: Fisher Exact** DM/diabetes meletus χ^2: **Chi square test**

p: p value for comparing between the two studied groups HTN/hypertention

*: Statistically significant at $p \leq 0.05$ PROM/premature rupture of membrane

Group A: Archive groupGroup B: New group

Table (4): Comparison between the two studied groups according to CBC parameters.

	CBC	**Without laminar (n=150)**	**With laminar (n=270)**	**U**	**P**
Cbc on admission	**WBCs x10^9/L**				
	Min. – Max.	2.0 – 45.0	2.40 – 55.20	20123.0	0.915
	SD.±Mean	8.22±14.28	7.70±14.11		
	Median (IQR)	12.70 (9.60–16.20)	12.80 (9.50–16.60)		
	Hb g/dl				
	Min. – Max.	6.0 – 22.0	6.0 – 17.40	19056.0	0.316
	SD.±Mean	3.21±15.52	4.20±15.76		
	Median (IQR)	15.45 (13.0–18.0)	15.20 (13.0–17.90)		
	PLTx10^9/l				
	Min. – Max.	0.0 – 701.0	0.0 – 701.0	18771.0	0.215

	SD.±Mean	125.12±211.71	120.25±221.49		
	Median (IQR)	208.0 (135.0–254.0)	215.0 (150.0–286.0)		
Cbc on discharge	**WBCs x10^9/L**				
	Min. – Max.	2.40 – 45.0	5.0 – 11.0		
	SD.±Mean	8.22±14.28	1.73±8.02	19620.0	0.597
	Median (IQR)	12.70 (9.60–16.20)	7.90 (6.7–9.40)		
	Hb g/dl				
	Min. – Max.	5.60 – 22.0	6.0 – 22.0		
	SD.±Mean	13.48 ± 3.21	3.21±15.52	12544.0*	<0.001*
	Median (IQR)	13.0 (11.10–16.0)	15.45 (13.0–18.0)		
	PLT x10^9/l				
	Min. – Max.	0.0 – 701.0	0.0 – 819.0		
	SD.±Mean	125.12±211.71	145.51±193.53	18417.0	0.124
	Median (IQR)	208.0 (135.0–254.0)	189.50 (69.0–275.0)		

U: Mann Whitney test WBC/white blood cells

p: p value for comparing between the two studied groups HB/hemoglobin

*: Statistically significant at $p \leq 0.05$ PLT/platelets

Group A: Archive groupGroup B: New group

Table (5): Comparison between the two studied groups according to electrolytes during parenteral nutrition.

Lab	Without laminar (n=150)	With laminar (n=270)	Test of sig.	P
Na^{+} meq/l				
Min. – Max.	130.0 – 150.0	130-150	t =0.470	0.639

SD.±Mean	5.64±140.29	4.64±140.53		
Median (IQR)	141.0 (135.0–145.0)	141.0(137.0–144.0)		
K^{+} meq/l				
Min. – Max.	3.70 – 6.50	3.30 – 6.40		
SD.±Mean	0.80±5.07	0.70±5.04	t=0.399	0.690
Median (IQR)	5.20 (4.40–5.70)	5.0 (4.50–5.60)		
Ca^{++} mg/dl				
Min. – Max.	5.90 – 10.0	5.90 – 11.2		
SD.±Mean	1.21±7.89	1.12±8.30	t=3.374*	0.001*
Median (IQR)	7.80 (6.80–9.0)	8.30 (7.50–9.10)		
ph^{+} mg/dl				
Min. – Max.	3.20 – 7.70	3.30 – 7.50		
SD.±Mean	1.31±5.66	1.20±5.47	t=1.509	0.132
Median (IQR)	5.70 (4.60–6.80)	5.60 (4.50–6.60)		

U: Mann Whitney test t: Student t-test

p: p value for comparing between the two studied groups

*: Statistically significant at $p \leq 0.05$

Group A: Archive groupGroup B: New group

Table (6): Comparison between the two studied groups according to liver function during parenteral nutrition.

Liver function	Without laminar (n=150)	With laminar (n=270)	Test of sig.	P
Albumin gm/dl				

Min. – Max.	1.70 – 4.20	1.70 – 4.20	t=3.687*	<0.001*
SD.±Mean	0.54±3.29	0.61±3.51		
Median (IQR)	3.30 (3.0–3.60)	3.60 (2.70–4.40)		
ALT U/L				
Min. – Max.	10.0 – 261.0	0.60 – 325.0	U= 13123.0*	<0.001*
SD.±Mean	43.28±23.94	44.49±23.74		
Median (IQR)	15.0 (12.0–17.0)	10.60 (7.10–17.0)		
AST U/L				
Min. – Max.	50.0 – 80.0	3.0 – 452.0	U= 15402.0*	<0.001*
SD.±Mean	8.98±64.93	52.29±65.49		
Median (IQR)	66.0 (56.0–73.0)	56.0 (37.0–74.0)		

U: Mann Whitney test t: Student t-test ALT/alanine transaminase

p: p value for comparing between the two studied groups AST/aspartate amino transferase

*: Statistically significant at $p \leq 0.05$

Group A: Archive groupGroup B: New group

Table (7): Comparison between the two studied groups according to cultures.

Cultures	**Without laminar (n=150)**		**With laminar (n=270)**		χ^2	**P**
	No.	**%**	**No.**	**%**		
Result						
No growth	119	79.3	221	81.9	3.589	$^{MC}p=$ 0.930
Actinobacterhumini	2	1.3	3	1.1		
Klebseilla	14	9.3	25	9.2		

Pseudomonus	1	0.7	3	1.1		
Staph aureus	3	2.0	7	2.6		
Staph epidermides	4	2.7	3	1.1		
Staph hominus	4	2.7	4	1.5		
Staph hemolyticus	3	2.0	4	1.5		
Antibiotic sensitivity						
No	119	79.3	221	81.9	0.397	0.529
Yes	**31**	**20.7**	**49**	**18.1**		
Tygacil	18	58.1	28	57.1	0.263	0.608
Linezolid	10	32.3	16	32.7	0.091	0.763
Vancomycin	12	38.7	18	36.7	0.258	0.611
Ciprofloxacin	6	19.4	8	16.3	0.322	0.571
Amikin	3	9.7	3	6.1	0.541	^{FE}p=0.671
Metronidazole	0	0.0	2	4.1	1.116	^{FE}p=0.540
SXT	0	0.0	2	4.1	1.116	^{FE}p=0.540
Azithromycin	2	6.5	2	4.1	0.359	^{FE}p=0.619

χ^2: **Chi square test** FE**: Fisher Exact**MC: **Monte Carlo**

p: p value for comparing between the two studied groups SXT/trimethoprim e sulfamethoxazole

Group A: Archive groupGroup B: New group

Table (8): Comparison between the two studied groups according to short term outcome.

	Without laminar (n=150)		**With laminar (n=270)**		**Test of sig.**	**P**
	No.	**%**	**No.**	**%**		
Sepsis						

No	55	36.7	156	57.8	χ^2= 17.191*	<0.001*
Yes	95	63.3	114	42.2		
Weight of discharge (kg)						
Min. – Max.	2.2-5.2		2.5-5.5		t=2.950	<0.003*
SD.±Mean	0.92±3.65		0.87±3.92			
Median (IQR)	3.60 (2.90-4.48)		3.90 (3.13–4.60)			

χ^2: **Chi square testU: Mann Whitney test**

p: p value for comparing between the two studied groups

*: Statistically significant at $p \leq 0.05$

Group A: Archive groupGroup B: New group

Table (9): Comparison between the two studied groups according to long term outcome.

Long term outcome	**Without laminar (n=150)**		**With laminar (n=270)**		**χ^2**	**P**
	No.	**%**	**No.**	**%**		
Neuro developmental delay						
No	119	79.3	248	91.9	22.15*	<0.001*
C.P	9	6	0	0		
Cerebral infarction	5	3.4	5	1.9		
Hydrocephalus	11	7.3	10	3.7		
Meningitis	6	4.0	7	2.5		
Bronchopulmonary dysplasia						
No	104	69.3	243	90.0	28.681*	<0.001*
Yes	46	30.7	27	10.0		

χ^2: **Chi square test** C.P/cerebral palsy

p: p value for comparing between the two studied groups

*: Statistically significant at $p \leq 0.05$

Group A: Archive groupGroup B: New group

IV. Discussion

The total number of neonates included in this study was 420. children from neonates, 150 neonates utilizig total parenteral nutrition prepared on ward the without laminar group, 60.7% were male and 39.3% were female. and 270 neonates uutilizing total parenteral nutrition prepared in our units the laminar group, 54.4% were male and 45.6% were female.

Our study showed that there are 270 cases on TPN unit with laminar, 150 cases without laminar. **Perez, et al.,**[**17**]mentioned that TPN with laminar was able to maintain neonatal temperature in the normal ranges, as well as securing low skin colonization in term, near term, and moderately preterm newborns. The advantage of using laminar flow in TPN units is to maintain neonatal temperature, but with added the advantages of isolation and humidification.

Regarding the demographic data our study concluded that there is highly significant decrease in weight of admission in the laminar group, the mean weight 3.03±0.68 In group without laminar and the mean weight 2.31±0.79 in the laminar group. But there is no significant difference between the two groups according to mode of delivery as that in group without laminar there were (24.7%) with NVD, (75.3%) with C.S. In group with laminar there were (21.5%) with NVD, (78.5%) with C.S.

This is in contrast to **Marofi et al.,** [**18**] who detected that there is no significant difference was found in neonates in terms of demographic characteristics. The two groups were similar in terms of (age, weight at the time of birth, gestational age, and neonates' age at TPN).

Our study showed that in the group without laminar there is (13.3%) with maternal problems, In group with laminar there is (21.9%) with maternal problems, and (16.9%) with premature rupture membrane (PROM). There is significant increase in the laminar as regard prescence of maternal problems especially PROM. But there is no significant difference between two groups as regard oxygen supply.

Although the study of **Nimrod et al.,** [**19**]showed thatFetuses delivered after PROM are at risk for lung hypoplasia because they lack amounts of amniotic fluid required for normal lung development.

Our study showed that there is increase in hemoglobin level in the laminar group.

We are similar to **Qiao et al.,** [**20**] who showed that Early parenteral nutrition, mostly from day 2of life, improved the Hb level and mean corpuscular volume (MCV) levels at 3 months of age.

Regarding to electrolytes our study concluded that in the group without laminar the mean Na+ 140.29 with, the mean K+ 5.07 the mean Ca++ 7.89 the mean ph+ 5.66 ,In the laminar group the mean Na+ 140.53,the mean K+ 5.04, the mean Ca++ 8.3 , the mean ph+ 5.47. There is significant increase in Ca++ level in the laminar group.

Yeung et al., [**21**] reported a series of 58 premature infants of gestational age below 33 weeks who received individualized or standard PN during the first week of life. For the standard group, intakes of calcium and phosphate were 25% greater than individualized group.

In our study showed that in the laminar group the mean albumin 3.51 ±0.61.the mean ALT 23.94 ± 43.28.the mean AST 64.93 ±8.98,and In the group without laminar the mean albumin 3.29 ±0.54,the mean ALT 23.74 ±44.49, the mean AST 65.49 ±52.29. There is significant increase in albumin level and improvement of liver function in the laminar group.

In agreement with us **Ziegler et al.,** [**22**]who found that a distinct improvement concerning amino acid supplies for the staderdized PN group with (+20%) increase.

Similar to us **Butler et al.,** [**23**] who detected that standardized parentral nutrition significantly increased amino acid and caloric intakes, and it reduced early weight loss than individualized type.

In The study of **Lenclen et al.,** [**24**] confirmed that production of standardized solutions by the pharmacy, designed for premature neonates, enables the improvement of early nutrient supplies, resulting in a greater amount of amino acids during the first week (20%), compared with infants receiving individualized formula (prepared by nurses in ward), and a better balance in the calcium phosphate ratio without any biological disorders.

Yeung et al., [**21**] also reported that neonates who received standard PN 42% improvement in gain amino acids than individualized group.

Compared with Individualized-PN and Standedized-PN **Smolkin et al.,** [**25**]confirmed that the complications such as PN abnormal liver function were not markedly different between the Individualized-PN and Standedized-PN groups, except for lower mean serum potassium, phosphorous and albumin values and higher serum alkaline phosphatase(ALP) in the individualized -PN group.

As regard blood culture Our study showed that in the group without laminar the most common organism was,(9.3%) klebsiella ,followed by staph ,then actinobacter and pseudomonas, In the laminar group the most common organism was klebsiella (9.2%), followed by staph , then actinobacter and pseudomonas.

Similar to our result **Pawa et al.,** [**26**] reported that klebsiella is the most common pathogen causing neonatal sepsis.

Other researchers like **Sastre et al.,** [**27**] found that klebsiella is the second common pathogen.

According to E.coli**Aurangzeb and Hameed**[**28**] showed that E. coli (77.1%) was the commonest organism in EONNS followed by Pseudomonas (8.9"/"), Klebsiella (7.4%), and Staphylococci (4.4%).and No E.coli reported by **Imtiaz et al.,** [**29**] from Lahore.la.

Regarding to sepsis and weight of discharge our study found that there is significant decrease in sepsis and significant increase in weight of discharge in the laminar group more than the without laminar group. This study showed that in group without laminar there were 95(63.3%) with develop sepsis the mean late weight 3.65 ±0.92,i n the without laminar group there were 114(42.2%) with develop sepsis the mean weight on discharge 3.92±0.87.

Similar to us the study of **Ziegler et al.,** [**22**] who suggested that poorly nourished infants who were gaining weight slowly might be more prone to late-onset infection.

We are similar to **Butler et al.,** [**23**]who showed that implementation of the standardized TPN resulted in improved outcomes for the patients with no increase in adverse outcomes from NEC, sepsis, mortality or line infections.in addition to achieving full enteral feeds in a significantly shorter time and regained birth weight.

Regarding to long term outcome our study showed that in the without laminar group there were 5(3.3%) with C.P. 20(13.3%) with hydrocephalus, 6 (4%) with meningitis, 46(30.7%) with bronchopulmonary dysplasia. In the laminar group there were 5(1.9%) with cerebral infarction, 10 (3.7%) with hydrocephalus, 7(2.5%) with meningitis, 27(10%) with bronchopulmonarydysplasia.there is increase in neurodevelopmental delay, and BPD between neonates in the without laminar group than the laminar group.

Those results were totally in agreement with **Ziegler et al.,** [**22**] suggested that poorly nourished infants were suffering from severe BPD. And suggested that the degree of undernutrition that occurs in many ELBW infants contributes to poor neurocognitive outcomes.

As regard **Lapillonne et al.,** [**30**]**found** thatEarly parenteral nutrition (nutrient-enriched formulas) support of preterm infants is critical to life-long health and well being. and have demonstrated that preterm infants are at increased risk of mortality and morbidity, including disturbances in brain development.

Also **Pallotto and Kilbride**[**31**] detected that Preterm infants that fail to catch-up growth as they took non computerized total parentral nutrition have increased risk for cognitive delays, decreased academic achievement and significantly increased risk of neurologic disorders in adult life

Similar to our results **Mihatsch et al.,** [**32**]who detected thatPoor nutritional status in critically ill neonates is associated with adverse clinical outcomes, increased in mortality rate.

V. Conclusion:

Early parenteral nutrition (PN) reduces the delay in weight gain In newborns. TPN with laminar flow unit is the cornerstone in prevention of complications and decrease mortality and morbidity in NICU as the laminar flow unit will achieve the following: Maintain neonatal temperature. Good isolation and humidification by havingclosed compartment intended for aseptic processing to avoid contamination.

Using laminar flow in TPN preparation decrease mortality rate ,occurance of neurodevelopmental delay ,bronchopulmonary dysplasia.

References:

[1] **Al-Salem, A. H. (2020):** Biliary Atresia. In Atlas of Pediatric Surgery (pp. 193-204). Springer, Cham.

[2] **Triantafillidis, J. K., and Papalois, A. E. (2013):** The role of total parenteral nutrition in inflammatory bowel disease: current aspects. Scandinavian journal of gastroenterology, 49(1), 3-14.

[3] **Evering, V. H., Andriessen, P., Duijsters, C. E., et al., (2017):** The effect of individualized versus standardized parenteral nutrition on body weight in very preterm infants. Journal of clinical medicine research, 9(4), 339.

[4]**Embleton, N. D., and Simmer, K. (2014):** Practice of parenteral nutrition in VLBW and ELBW infants. In Nutritional Care of Preterm Infants (Vol. 110, pp. 177-89). Karger Publishers.

[5]**Riskin, A., Picaud, J. C., Shamir, R., et al., (2018):**espghan/ espen/ espr/ cspen guidelines on pediatric parenteral nutrition: Standard versus individualized parenteral nutrition. Clinical Nutrition, 37(6), 2409-17.

[6] **Bouchoud, L., Fonzo-Christe, C., Sadeghipour, F., et al., (2010):** Maximizing calcium and phosphate content in neonatal parenteral nutrition solutions using organic calcium and phosphate salts. Journal of Parenteral and Enteral Nutrition, 34 (5), 542-5.

[7] **White, R. (2011):** Quality parenteral nutrition: an ideal mixed bag. Proceedings of the Nutrition Society, 70(3), 285-92.

[8]**Sommer, I., Bouchoud, L., Berger-Gryllaki, M, et al., (2020):** Quality and safety of parenteral nutrition for newborn and preterm infants as an on-ward preparation. European Journal of Hospital Pharmacy, 27(5), 292-6.

[9] **De Sanctis, R., Coratti, G., Pasternak, A., et al., (2016):** Developmental milestones in type I spinal muscular atrophy. Neuromuscular Disorders, 26(11), 754-9.

[10]**Voytas, L. (2018):** Beyond the Checkup from Birth to Age Four: A Pediatrician's Guide to Calm, Confident Parenting. Sasquatch Books.

[11]**Riskin, D. J., Longaker, M. T., Gertner, M., et al.**, **(2006)**: Innovation in surgery: a historical perspective. Annals of surgery, 244(5), 686.

[12] **Ballard, J. L., Khoury, J. C., Wedig, K. L., et al., (1991):** New Ballard Score, expanded to include extremely premature infants. The Journal of pediatrics, 119(3), 417-23.

[13] **Torres, M. T., Valstar, M. F., Henry, C., et al., (2017):** Small sample deep learning for newborn gestational age estimation. In 2017 12th IEEE International Conference on Automatic Face and Gesture Recognition (FG 2017) (pp. 79-86). IEEE

[14]**Guerti, K., Devos, H., Ieven, M. M., et al., (2011):** Time to positivity of neonatal blood cultures: fast and furious?. Journal of medical microbiology, 60(4), 446-53.

[15] **Thomson, J., Sucharew, H., Cruz, A. T., et al., (2018):** Cerebrospinal fluid reference values for young infants undergoing lumbar puncture. Pediatrics, 141(3).

[16] **Albers, M. J. (2017):** Quantitative data analysis—In the graduate curriculum. Journal of Technical Writing and Communication, 47(2), 215-33.

[17] **Perez, J. M., Golombek, S. G., Fajardo, C., et al., (2013):** A laminar flow unit for the care of critically ill newborn infants. Medical Devices (Auckland, NZ), 6, 163.

[18]**Marofi, M., Bijani, N., Abdeyazdan, Z., et al., (2017):** The impact of an educational program regarding total parenteral nutrition on infection indicators in neonates admitted to the neonatal intensive care unit. Iranian journal of nursing and midwifery research, 22(6), 486.

[19] **Nimrod, C., Varela-Gittings, F., Machin, G., et al., (1984):** The effect of very prolonged membrane rupture on fetal development. American journal of obstetrics and gynecology, 148(5), 540-3.

[20]**Qiao, L., Tang, Q., Zhu, W., et al., (2017):** Effects of early parenteral iron combined erythropoietin in preterm infants: A randomized controlled trial. Medicine, 96(9).

[21]**Yeung, M. Y., Smyth, J. P., Maheshwari, R., et al., (2003):** Evaluation of standardized versus individualized total parenteral nutrition regime for neonates less than 33 weeks gestation. Journal of paediatrics and child health, 39(8), 613-7.

[22] **Ziegler, E. E., Thureen, P. J., and Carlson, S. J. (2002):** Aggressive nutrition of the very low birthweight infant. Clinics in perinatology, 29(2), 225-44.

[23] **Butler, T. J., Szekely, L. J., and Grow, J. L. (2013):** A standardized nutrition approach for very low birth weight neonates improves outcomes, reduces cost and is not associated with increased rates of necrotizing enterocolitis, sepsis or mortality. Journal of Perinatology, 33(11), 851-7.

[24]**Lenclen, R., Crauste-Manciet, S., Narcy, P., et al., (2006):** Assessment of implementation of a standardized parenteral formulation for early nutritional support of very preterm infants. European journal of pediatrics, 165(8), 512-8.

[25]**Smolkin, T., Diab, G., Shohat, I., et al., (2010):** Standardized versus individualized parenteral nutrition in very low birth weight infants: a comparative study. Neonatology, 98(2), 170-8.

[26]**Pawa, A. K., Ramji, S., Prakash, K., et al., (1997):** Neonatal nosocomial infection: profile and risk factors. Indian pediatrics, 34, 297-302.

[27]**Sastre, J. L., Cotallo, D. C., Colomer, B. F., et al., (2002):** Neonatal sepsis of nosocomial origin: an epidemiological study from the" Grupo de HospitalesCastrillo". Journal of perinatal medicine, 30(2), 149-57.

[28] **Aurangzeb, B., and Hameed, A. (2003):** Neonatal sepsis in hospital-born babies: bacterial isolates and antibiotic susceptibility patterns. journal-college of physicians and surgeons of pakistan, 13, 629-32.

[29]**Imtiaz, M. J., Izhar, T. S., and Akmal, N. (1997):** Maternal risk factors in early onset septicemia. Pak Paediatr J, 21, 81-5.

[30]**Lapillonne, A., Carnielli, V. P., Embleton, N. D., et al., (2013):** Quality of newborn care: adherence to guidelines for parenteral nutrition in preterm infants in four European countries. BMJ open, 3(9).

[31]**Pallotto, E. K., and Kilbride, H. W. (2006):** Perinatal outcome and later implications of intrauterine growth restriction. Clinical obstetrics and gynecology, 49(2), 257-69.

[32]**Mihatsch, W., Fewtrell, M., Goulet, O., et al., (2018):**espghan/espen/ espr/ cspen guidelines on pediatric parenteral nutrition: Calcium, phosphorus and magnesium. Clinical Nutrition, 37(6), 2360-5