



## COMPLICATIONS DURING THE THERAPEUTIC PLASMA EXCHANGE

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**ABSTRACT** Therapeutic apheresis is the treatment of diseases through removal or extracorporeal manipulation of blood components or specific blood substances. In this we were observe the complications during the procedure with respect to patient's demographic profiles and procedural variations in one-year. In our study total 60 cases and total 150 TPE cycles were performed the mean age of total patients was 31.95±11.66. Female dominance was observed [78(52%)] over males [72(48%)]. Overall, 56(71.79%) females were observed without complications however 22(28.21%) were observed with complications. Maximum pulse rate was observed during the procedure (97.05±8.30), maximum systolic blood pressure(SBP) was observed at pre-procedure (121.43±17.28), maximum diastolic blood pressure(DBP) was also observed at pre-procedure (85.93±7.06), maximum respiratory rate(RR) was reported during the procedure (25.40±12.87) and maximum oxygen saturation(SPO2) was reported before start the procedure (98.64±2.42). Maximum mean variation of pulse was observed itching (38±20), followed by hypothermia (28.50±12.60). Maximum mean variation of SBP was observed for itching (15±5), followed by tingling sensation over all body (10±00). Maximum mean variation of DBP was observed for nausea (5±5). Maximum mean variation of RR was observed itching (8.50±4.50). Maximum mean variation of SPO2 was observed for tingling sensation over all the body (2±00). Complication during the procedure primarily in females with a correlation with BMI. With respect to procedural variation, the most common complication was itching followed by a tingling sensation over all the body in correlation with Pulse Rate, Systolic BP, Diastolic BP, Respiratory Rate, and SPO<sub>2</sub>. All the complications were mild and manageable.

**KEYWORDS :** Therapeutic Plasma Exchange, Fresh Frozen Plasma, Demographic profile, Immediate Complications, Procedural variations.

**INTRODUCTION:**

Apheresis (plural aphereses; from the ancient Greek aphaire-sis, "a taking away") is a procedure in which whole blood is removed from the body and passed through an apparatus that separates out one (or more) particular blood constituent. It then returns the remainder of the constituents to the individual's circulation. Through the use of sophisticated automation, an apheresis procedure can be performed on either a blood donor or a patient.(1) Therapeutic apheresis is the treatment of diseases through removal or extracorporeal manipulation of blood components or specific blood substances. It is distinct from blood component collection by apheresis. The goal of therapeutic apheresis is to remove a pathologic element from blood or to modulate cellular function by manipulation such as through extracorporeal photopheresis with or without replacement of the removed element.(2)

**AIMS AND OBJECTIVES:**

To study the complications during the procedure with respect to patients' demographic profile and procedural variations.

**MATERIAL AND METHODS:**

This is a one year prospective observational study conducted by Department of Transfusion Medicine in collaboration with Medicine Department, King George' Medical University, Lucknow. This included all the patients, who required TPE, as a part of their management Plasmapheresis is indicated in the conditions mediated by plasma factors such as autoantibodies, immune complex, drugs or toxins bound to proteins, high cholesterol or triglycerides. Plasma exchange is done on the request of the patient's physician. who fulfilled criteria for TPE as per the guidelines laid down by Directorate General Health Services (DGHS), Ministry of Health and Family Welfare, Government of India and Drugs and Cosmetics Act, 2020 were included in the study.(3)

Institutional ethics committee approval will be obtained before commencement of the study. Central line vein is the most preferable vein, in some cases femoral veins will also be assessed for their suitability for phlebotomy.

Therapeutic Plasma Exchange procedures were performed TPE will be performed on COM .TEC, Fresenius Kabi, Germany\* by using TPE Kit, it is a Closed system, TPE Fresenius Kabi, Germany\* and anticoagulant ACD Fresenius Kabi, Germany\*. Normally the range of anticoagulant ACD ratio, will be used during the TPE cycle is 1:8 to 1:12. The range of the blood flow, will use during the TPE procedure is 30 to 50 ml/min. (4) In the whole procedure, we were observed the patient very carefully, recorded all the complications if it will be manifested during the procedure. The Immediate complications may be like :- nausea, vomiting, itching, tachycardia, anxiety, lightheadedness, numbness of limbs, bleeding and hematoma, blockage of tubing in TPE kit, dyspnea, dizziness, dislocation of needle at the phlebotomy site, burr wheezings, sensation of being cold, chills, tremors, hypotension, hypovolemia, hypocalcemia etc.(5)

We were calculated, plasma volume has to be replaced from FFP. Before starting the procedure informed consent form were taken from the patient's attendants. Introduced patient's attendants about the TPE procedure and related to all complications if came due to the procedure. Instruct the patient if he/ she was conscious and well oriented tell us, any kind of problem felt. Also taken preprocedural vitals, mid of the procedure vitals and postprocedure vitals. If any kind of complications were came during the procedure noted all and managed prophylactically by injection calcium gluconate, injection Avil, injection ondansetron. At the end procedure, return all the blood components (auto re-infuse) remaining in the TPE kit. Detached the kit from the cell separator with waste plasma and discard it, according to BMW guidelines as per our institutional SOP.(6)(7)

**RESULTS:**

In our study we were observed complications during the TPE on total 60 cases and total 150 TPE cycles performed on those who required TPE, as a part of their management. The mean age of total enrolled patients was 31.95±11.66. The most prevalent age group was 30-49 years with maximum number of patients [78(52%)] followed by 10-29 years [66(44%)] and so on. Further, female dominance was observed [78(52%)] over males [72(48%)] along with statistically insignificant difference among them. Furthermore, majority of enrolled patients

reported to have BMI>30 [126(84%)], followed by 25.00-29.99 [22(14.67%)] and so on. [Table 1]

Out of 150 total patients, 110 (73.33%) patients reported with no complications. However out of patients having complications, maximum patients [12(8%)] reported to have nausea, allergy and cough, followed by allergy [10(6.67%)] and so on [Figure 2]

We were observed, the age distribution based on the complication during procedure. Maximum mean age (55±25) was observed for tingling sensation overall body, followed by mean age (43.75±22.74) for Nausea and so on. [Figure 3]

We were observed, the gender distribution based on the complication during the procedure. Overall 56(71.79%) females were observed without complications however 22(28.21%) were observed with complications. Similarly, 54(75%) males were observed without complications and 18(25%) males were observed with complications. [Figure 4]

We were observed mean BMI of total enrolled patients based on the complication during the procedure. Maximum mean BMI was observed for tingling sensation overall the body (40±5.71), followed by Allergy (36.61±5.90) and so on. [Table 5]

While observing the vital comparison among pre and during procedural variations we have found that maximum pulse rate was observed during the procedure (97.05±8.30), maximum SBP was observed at pre-procedure (121.43±17.28), maximum DBP was also observed at pre-procedure (85.93±7.06), maximum RR was reported during the procedure (25.40±12.87) and maximum SPO2 was reported before the start of the procedure (98.64±2.42). [Figure 6]

We were observed the mean variation of the pulse, based on the complication during the procedure. Maximum mean variation of pulse was observed for itching (38±20), followed by hypothermia (28.50±12.60) and so on. [Table 7]

We were observed the mean variation of the SBP, based on the complication during the procedure. Maximum mean variation of SBP was observed for itching (15±5), followed by tingling sensation over all body (10±00) and so on. [Figure 8]

We were observed the mean variation of the DBP, based on the complication during the procedure. Maximum mean variation of DBP was observed for nausea (5±5). [Table 9]

We were observed the mean variation of the RR, based on the complication during the procedure. Maximum mean variation of RR was observed for itching (8.50±4.50). [Table 10]

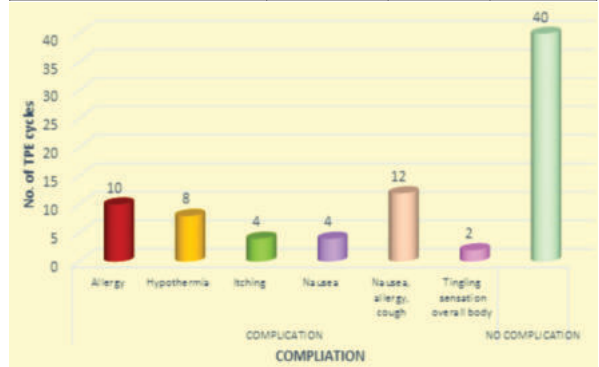
We were observed the mean variation of the SPO2, based on the complication during the procedure. Maximum mean variation of SPO2 was observed for tingling sensation over all the body (2±00). [Table 11]

In our study we were observed the correlational analysis during the procedure among complications and other parameters. We have observed that during procedure positive correlation was observed among complication Vs all parameters except, Pulse (r= -0.206) and SPO2 (r=-0.01895). [Table 12]

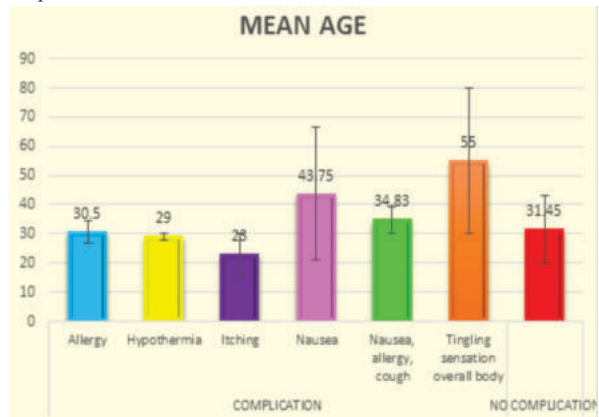
**Table 1: Tabular presentation of the demographical parameters for total patients.**

Demographical Parameters	Mean	%	P- Value
AGE Year			
10-29	66	44.00%	X=81.25 p<0.0001
30-49	78	52.00%	
50-69	2	1.33%	
70-89	4	2.67%	
MEAN±SD	31.95±11.66		
GENDER			
Female	78	52.00%	X=0.1200
Male	72	48.00%	p=0.7290
HEIGHT	164.92	8.18	---
WEIGHT	57.39	10.04	
BMI Kg/m <sup>2</sup>			

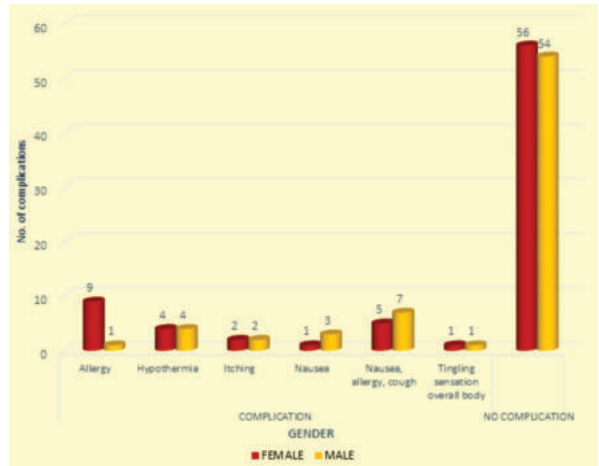
18.50-24.99	2	1.33%	X=88.01 p<0.0001
25.00-29.99	22	14.67%	
> 30.00	126	84.00%	



**Figure 2:** Graphical presentation of the complications observed during the procedure



**Figure 3:** Graphical presentation of age distribution based on the complication during procedure.



**Figure 4:** Graphical presentation of the gender distribution based on the complication during procedure.

**Table 5: Tabular presentation of the BMI distribution based on the complication during procedure.**

COMPLICATION		BMI Kg/m <sup>2</sup>	
		MEAN	SD
YES	Allergy	36.62	4.81
	Hypothermia	30.39	3.90
	Itching	28.81	5.48
	Nausea	36.01	5.90
	Nausea, allergy, cough	34.95	4.26
	Tingling sensation overall body	40.00	5.71
With Complication		34.20	5.64
No Complication		34.84	4.86
P- Value		t=1.053 p=0.2933	

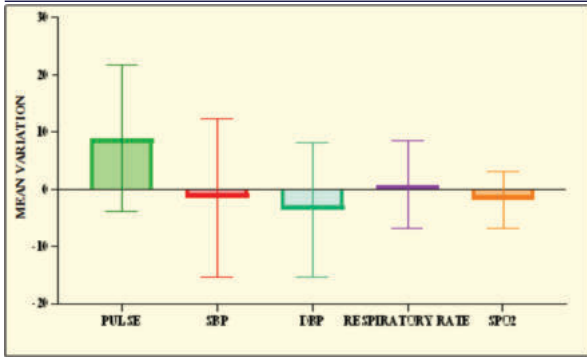


Figure 6: Graphical presentation of the vitals in respect of procedural variations.

Table 7: Tabular presentation of the complications based on the mean variation pulse.

Complication		Mean Variation Of Pulse [In during the procedure]	
		MEAN	SD
YES	Allergy	0.00	1.79
	Hypothermia	28.50	12.60
	Itching	38.00	20.00
	Nausea	9.00	9.00
	Nausea, allergy, cough	4.00	5.03
	Tingling sensation overall body	2.00	0.00
Total Complication		11.70	16.47
No Complication		7.88	10.96
Overall Mean Variation		8.90	12.78
P- Value		t=2.365	p=0.0187

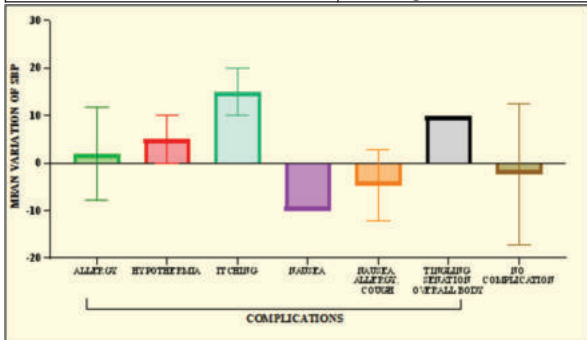


Figure 8: Graphical presentation of the complications based on the mean variation SBP.

Table 9: Tabular presentation of the complications based on the mean variation DBP.

Complication		Mean Variation Of DBP [In during the procedure]	
		MEAN	SD
YES	Allergy	-4.00	8.00
	Hypothermia	0.00	0.00
	Itching	-45.00	0.00
	Nausea	5.00	5.00
	Nausea, allergy, cough	-1.67	6.87
	Tingling sensation overall body	0.00	0.00
TOTAL COMPLICATION		-5.50	14.57
NO COMPLICATION		-2.89	10.36
OVERALL MEAN VARIATION		-3.59	11.69
P-VALUE		t=1.788	p=0.0748

Table 10: Tabular presentation of the complications based on the mean variation RR.

COMPLICATION		Mean Variation Of Respiratory Rate [In during the procedure]	
		MEAN	SD
YES	Allergy	0.00	0.00
	Hypothermia	6.75	11.69
	Itching	8.50	4.50

	Nausea	1.00	1.00
	Nausea, allergy, cough	-1.33	1.49
	Tingling sensation overall body	0.00	0.00
TOTAL COMPLICATION		1.90	6.59
NO COMPLICATION		0.42	7.98
OVERALL MEAN VARIATION		0.81	7.67
P-VALUE		t=1.751	p=0.0809

Table 11: Tabular presentation of the complications based on the mean variation SPO2.

COMPLICATION		Mean Variation Of SPO2 [In during the procedure]	
		MEAN	SD
YES	Allergy	0.00	1.26
	Hypothermia	-3.00	3.67
	Itching	-8.00	5.00
	Nausea	-1.00	1.00
	Nausea, allergy, cough	0.00	0.00
	Tingling sensation overall body	2.00	0.00
TOTAL COMPLICATION		-1.40	3.50
NO COMPLICATION		-2.00	5.45
OVERALL MEAN VARIATION		-1.84	5.01
P-VALUE		t=1.135	p=0.2575

Table 12: Tabular presentation of the correlational analysis during the procedure among complications and other parameters.

CORRELATION ANALYSIS (DURING THE PROCEDURE)			
COMPLICATIONS VS.	Spearman r	95% confidence interval	P value
Pulse(bpm)	-0.206	-0.3588 to -0.04256	0.0114
Systolic BP(mmHg)	0.1097	-0.05627 to 0.2697	0.1816
Diastolic BP(mmHg)	0.1091	-0.05682 to 0.2692	0.1838
Respiratory Rate(breath per min)	0.1272	-0.03855 to 0.2861	0.1209
O <sub>2</sub> Saturation(%)	-0.01895	-0.1833 to 0.1464	0.8179
BMI(Kg/m <sup>2</sup> )	0.02862	-0.1369 to 0.1926	0.7281

**DISCUSSION:**

Therapeutic plasma exchange (TPE) is the procedure in which a large volume of plasma is removed from a patient. The volume removed is such that if it were not replaced, significant hypovolemia resulting in vasomotor collapse would occur. As a result, the removed plasma must be replaced with some form of replacement fluid.(8)

According to N. Basic-Jukic, P. Kes, S. Glavas-Boras et al.(2005).(9) study 509 patients, or 4857 PE treatments, was retrospectively analyzed to test the safety of PE. A total of 231 adverse reactions were recorded (4.75% of treatments). The most common complications were pares- thesia (2.7%), hematoma at the puncture site (2.4%), clot- ting (1.7%), mild to moderate allergic reactions (urticaria; 1.6%) and bleeding (0.06%). True anaphylactoid reactions were recorded in five procedures. The incidence of severe, potentially life-threatening adverse reactions was 0.12%. According to M. Henriksson, E. Newman, V. Witt et al.(2016)(10) reported that more AEs occurred during the first procedures versus subsequent (8.4 and 5.5%, respectively). AEs were mild in 2.4% (due to access 54%, device 7%, hypotension 15%, tingling 8%), moderate in 3% (tingling 58%, urticaria 15%, hypotension 10%, nausea 3%), and severe in 0.4% of procedures (syncope/hypotension 32%, urticaria 17%, chills/fever 8%, arrhythmia/ asystole 4.5%, nausea/vomiting 4%). According to F. Alalawi, A.Seddik, K.Gulzar et al. (11) study, complications occurred in 2 sessions out of 142 sessions (1.4%); allergic reaction to IVIG given after the session of TPE in post kidney transplant patient with acute allograft rejection and lastly volume overload, resulted from replacement fluid in a patient with acute pancreatitis and Hypertriglyceridemia. In our study,we were observed complications during the procedure, Out of 150 total TPE cycles, 110 (73.33%) cycles reported with no complications. Maximum complications [12(8%)] reported to have nausea, allergy and cough, followed by allergy [10(6.67%)]. Overall statistically significant (p<0.0001) difference was observed among both the groups patients having complications and those who don't have. [Figure 2]

According to S. Ghosh, L. Paton et al. (1985)(12) study, The incidence of pruritus and urticaria was higher in children of the 6 ~ 15



year group ( $P < 0.05$ ) compared with other age groups. In our study we were observed, Maximum mean age ( $55 \pm 25$ ) was observed for tingling sensation overall body, followed by mean age ( $43.75 \pm 22.74$ ) for Nausea and so on, along with statistically insignificant difference among them. [Figure 3]

According to C. Taylan, A.Schaaf, C.Dorn et al. (13) study, Female gender was associated with a higher general complication rate ( $p = 0.03$ ) in the univariate analysis. No correlation between female gender and a specific type of complications was found: catheter dysfunctions ( $p = 0.08$ ), non-specific/non-allergic events ( $n = 0.39$ ), allergic reactions ( $p = 0.43$ ), clotting/bleeding ( $p = 0.44$ ) and other complications ( $p = 0.52$ ). In the multivariate analysis, the gender effect could not be confirmed. In our study, we were observed, Overall 56(71.79%) females were observed without complications, however 22(28.21%) were observed with complications. Similarly, 54(75%) males were observed without complications and 18(25%) males were observed with complications, along with statistically insignificant difference among them. So that we were found maximum complications in females during the procedure. [Figure 4]

According to S. Ghosh, L. Paton, (12) study, showed that the incidence of complications in the 6 ~ 15 year group was higher than that in the 0 ~ 3 year and 3 ~ 6 year groups, and the incidence of complications in the 30 ~ 60kg group was still higher than that in the 0 ~ 10kg group and 10 ~ 30kg groups. Older age group appears higher complications, it may be related to higher dosage of plasma, the more plasma is used, the more susceptible to allergy. In our study, maximum mean BMI was observed for tingling sensation overall the body ( $40 \pm 5.71$ ), followed by Allergy ( $36.61 \pm 5.90$ ), along with statistically insignificant difference among them. [Table 5]

According to J. Lu, L. Zhang, C. Xia et al. (2019) (14) reported that there was no significant difference in the incidence of hypertension and hypotension in children at different ages and weights ( $P > .05$ ). While in our study we were observed the vital comparison among pre and during procedural variations we have found that maximum pulse rate was observed during the procedure ( $97.05 \pm 8.30$ ), maximum SBP was observed at pre-procedure ( $121.43 \pm 17.28$ ), maximum DBP was also observed at pre-procedure ( $85.93 \pm 7.06$ ), maximum RR was reported during the procedure ( $25.40 \pm 12.87$ ) and maximum SPO<sub>2</sub> was reported before the start of the procedure ( $98.64 \pm 2.42$ ). Further, overall statistically significant difference was observed among all the noted vitals for all three categories. [Figure 6]

In our study we were observed, the maximum mean variation of pulse was observed for itching ( $38 \pm 20$ ), followed by hypothermia ( $28.50 \pm 12.60$ ) and so on, along with statistically significant difference among them ( $p = 0.0187$ ). [Table 7]

According to M. Mokrzycki, A. Kaplan, N. Basic-Jukic et al. (15) study, The mean systolic blood pressure dropped significantly during the TPE treatment, from  $140 \pm 24$  ( $P < 0.0001$ ). The decline in systolic blood pressure mmHg pretreatment to  $133 \pm 22$  mmHg posttreatment was more pronounced in patients receiving albumin, saline, whose systolic blood pressure declined from a mean of  $144 \pm 25$  mmHg to  $134 \pm 23$  mmHg, than in patients receiving FFP, whose systolic blood pressure dropped from  $136 \pm 21$  to  $132 \pm 21$  mmHg ( $P < 0.0001$ ). Neither the pretreatment or the posttreatment blood. In our study we were observed the maximum mean variation of SBP was observed for itching ( $15 \pm 5$ ), followed by tingling sensation over all body ( $10 \pm 00$ ) and so on, along with statistically significant difference among them ( $p = 0.0171$ ). [Figure 8] We were also observed the mean variation of the DBP, based on the complication during the procedure. Maximum mean variation of DBP was observed for nausea ( $5 \pm 5$ ), along with statistically insignificant difference among them. [Table 9]

According to Michele H. Mokrzycki MD, Andre A. Kaplan (15) study, the 15,658 procedures reported in the literature, reveals that serious complications do not commonly occur. These are characterized by cardiovascular events (0.2%), respiratory events (0.2%), and anaphylactoid reactions (0.25%). In our study we were observed the maximum mean variation of RR was observed for itching ( $8.50 \pm 4.50$ ), along with statistically insignificant difference among them. [Table 10]

According to E. M. Kfoury Baz, M.F. Khatib et al. (16) study, The ratio of the oxygen saturation by pulse oxymetry (SpO<sub>2</sub>) to the fraction of inspired oxygen (FiO<sub>2</sub>) was calculated before, during and after TPE. In these five patients with lung disorders, there was a consistent trend

of a decreasing SpO<sub>2</sub>/FiO<sub>2</sub> quotient during and within 2 h post TPE compared to the pre-TPE value. The decrease in SpO<sub>2</sub>/FiO<sub>2</sub> range was 0.20-0.89 with an average of 0.56. In our study we were observed the maximum mean variation of SPO<sub>2</sub> was observed for tingling sensation over all the body ( $2 \pm 00$ ), along with statistically insignificant difference among them. [Table 11]

In our study we were observed the correlational analysis during the procedure among complications and other parameters. We have observed that during procedure positive correlation was observed among complication Vs all parameters except, Pulse ( $r = -0.206$ ) and SPO<sub>2</sub> ( $r = -0.01895$ ). However the significant association was observed only for Complication vs Pulse ( $p = 0.0114$ ) [Table 12]

## CONCLUSION:

Complication during the procedure was mainly allergy, nausea, and cough primarily in females with a correlation with BMI. With respect to procedural variation, the most common complication was itching followed by a tingling sensation over all the body correlation with Pulse Rate, Systolic BP, Diastolic BP, Respiratory Rate, SPO<sub>2</sub>. We found that adverse events at initial therapeutic plasma exchange using FFP occurred frequently. As per the results adverse events were mild to moderate were managed by conservative treatment. So, overall therapeutic plasma exchange is generally safe and well tolerated procedure.

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