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## Aims & Scope

The Journal aims to publish research in all fields of clinical, diagnostic, experimental & preventive areas related to medical sciences to disseminate scholastic work among clinicians and scientists around the globe.



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Editorial

# INDUCED PLURIPOTENT STEM CELLS FOR DEVELOPMENT OF CANCER IMMUNOTHERAPY- A VIABLE IDEA FOR LESS TOXIC TREATMENT

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**ABSTRACT**
Induced pluripotent stem cells were introduced by Prof. Yamanaka and now being studied in all stem cells related treatment methods. Cancer immunotherapy is now part of targeted therapy and showing promising results, however the cost of treatment and tagged risk of side effects making it difficult for patients. Thus use of induced pluripotent stem cells to grow into plasma cells and produce antibodies against cancer targets will be a breakthrough in cancer management

**Key Words**: Cancer immunotherapy, Induced pluripotent stem cells, stem cell research

## INTRODUCTION

Cancer has remained a deadly disease from the ancient period. The earliest reported information dates back to 3000 B.C. when Edwin Smith Pyparus reported eight breast cancer cases and defined them as an ailment for which there was no treatment(1). Following the establishment of first cancer hospital in France and second in Great Britain in 18th Century, paved a way for organized data collection(1). During early 19th century the clinicians and scientists discovered that there are a number of factors which control the prognosis of the cancer (2–4). This discovery then resulted in exploration of treatment options including local therapy (ie surgery and radiotherapy) and systemic therapy (ie chemotherapy, endocrine therapy and immunotherapy).

The developed countries have now moved towards the translational research where the treatment targets are discovered in the laboratory and are utilized in clinical practice to predict fate of the disease. As a result cancer is now more manageable in the developed countries with much better prognosis. Since the inception of the concept of Precision medicine now more discoveries in the field of cancer sciences are also expected.

## CANCER RESEARCH IN PAKISTAN

Pakistan is still at the primitive stage of cancer research. According to the cancer statistics reported by World Health Organization Project Golobocon 2020 Pakistan is having the highest incidence of breast cancer among Asian countries same is the prevalence of some other forms of cancer too(5). Our local data suggest very high prevalence of oral cancers in interior Sindh contributing to 27% of all cancer reported in the region. Although the incidence of many cancers is lower in Pakistan as compared to the developed countries but the mortality is high(5). The major reason for the high mortality appears

to be the lack of any national guidelines based on evidence based local research conducted on our own patients. It is essentially important to understand the genetics and molecular attributes of cancer cell/ tissues in our own society so that locally appropriate tailored treatment policies can be adopted. With the same token it would also be possible to produce medicines in Pakistan well according to dominant cancer pattern. In future this will not only improve cancer management but will surely help in introducing more effective and economical cancer treatment options.

## CANCER IMMUNOTHERAPY

The immunotherapy (ie monoclonal antibodies) widely used in cancer therapeutics and showing great success in controlling the disease even at advance stage. First of its kind medicine in breast cancer was trastuzumab. However, the cost involved is too much on the family as well as pose great economic burden on the country. Currently available immunotherapeutic drugs are being used not only in cancers but other diseases such as autoimmune disorders as well.

## Anti-cancer Vaccine development from induced pluripotent stem cells

Cancer antibodies are being produced against the identified targets in the cancer cells such as HER2 receptor, EGFR, VEGF etc. These are being developed from animal sources, with chances of toxic effects and less efficacy. The stem cells on the other hand, have been used for organ generation and showing promising potential of great success in future. Thus production of blood cells from stem cells will be an important landmark.

These are re-programed adult cells to go into pluripotent stage and become plasma cells to produce antibodies(6). The technique was developed by Prof. Yamanaka, who won Nobile prize for this achievement. This technique is absolutely amazing to revolutionize cancer treatment. The work is also underway to look at the potential of induced pluripotent stem cells in hematological disorders(7). There is limited work done on use of induced pluripotent cells to produce antibodies. Though it is a novel idea of developing vaccine from induced pluripotent stem cells where adult B cells will be treated to go into pluripotent stage and then transform into plasma cells having potential of production of specific antibodies targeting cancer proteins. The research is needed for specific methods to develop these human monoclonal antibodies. This will provide precision medicine in its true sense and also reduce the number of side effects produced by humanized antibodies which are actually animal origin.

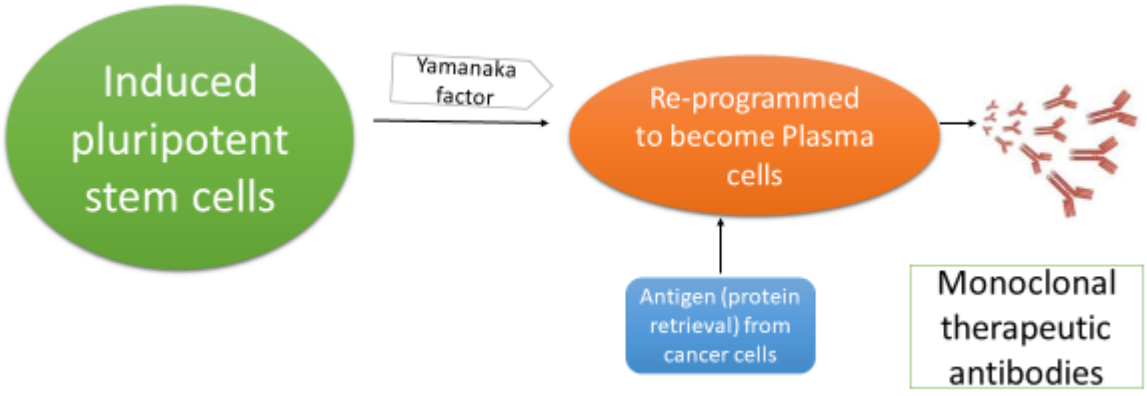


**Figure 1: Proposed plan for production of anti-cancer anti-bodies from induced pluripotent stem cells**

## REFERENCES


1. Bloom HJG, Richardson WW, Harries EJ. Natural history of untreated breast cancer (1805-1933). Br Med J. 1962;2(5299):213–21.
2. Kwon J, Eom KY, Koo TR, Kim BH, Kang E, Kim SW, et al. A prognostic model for patients with triple-negative breast cancer: Importance of the modified nottingham prognostic index and age. J Breast Cancer. 2017;20(1):65–73.
3. Syed BM, Green AR, Paish EC, Soria D, Garibaldi J, Morgan L, et al. Biology of primary breast cancer in older women treated by surgery: With correlation with long-term clinical outcome and comparison with their younger counterparts. Br J Cancer. 2013;
4. Fayaz Hussain Mangi, Jawaid Naeem Qureshi. Validation of onco-assist survival prediction tool in stage I, II and IIIcolon cancer among Asian patients. LIAQUAT Med Res J [Internet]. 2021 Dec 31;3(4):107–11. Available from: http://121.52.154.205/index.php/LMRJ/article/view/808
5. GLOBOCAN 2020: New Global Cancer Data | UICC.
6. Aboul-Soud MAM, Alzahrani AJ, Mahmoud A. Induced Pluripotent Stem Cells (iPSCs)—Roles in Regenerative Therapies, Disease Modelling and Drug Screening. Cells [Internet]. 2021 Sep 5;10(9):2319. Available from: https://www.mdpi.com/2073-4409/10/9/2319
7. Georgomanoli M, Papapetrou EP. Modeling blood diseases with human induced pluripotent stem cells. Dis Model Mech [Internet]. 2019 Jun 1;12(6). Available from: https://journals.biologists.com/dmm/article/12/6/dmm039321/3333/Modeling-blood-diseases-with-human-induced

Research article

# HYPERPROLACTINEMIA IN NEWLY DIAGNOSED BREAST CANCER IN YOUNGER (UNDER 50 YEARS) WOMEN

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**ABSTRACT**

Breast cancer is a common malignancy among women. There are a number of established risk factors for breast cancer in younger population. Hyperprolactinemia is observed to be higher in breast cancer patients. However its presentation in younger (<50 years) women is not well understood. This study was conducted to describe serum prolactin level in newly diagnosed breast cancer patients presented with nipple discharge without any apparent other cause of hyperprolactinemia. The results showed high serum prolactin levels in all these patients. There was no significant correlation observed between serum prolactin and the age of the patients.

It was concluded that breast cancer patients presenting with nipple discharge show varying degree of hyperprolactinemia. It requires further studies to explore if it has a causal relationship or it is a feature of breast cancer.

**Key Words**: Breast cancer, Prolactin, Hyperprolactinemia

## INTRODUCTION.

Prolactin is an important hormone released from the pituitary gland and responsible for breast development, milk production and lactation. The hormone plays an important role in the breast development even in utero(1). On the other hand, breast cancer is the leading cancer in women and the rate is expected to rise more in future(2). Pakistan has a rising trend of breast cancer in the younger population and associated with high mortality.

The primary site of prolactin production is pituitary gland but breast tissue has also capability to produce prolactin locally. Normal/ physiological rise in prolactin is seen in pregnant women and during lactation, advancing age also showed higher prolactin levels.

Hyperprolectinemia is reported to occur more commonly in females with a reported rate of 1% of population(3). Most common cause of hyperprolectenemia is pituitary adenoma, additionally certain drugs and systemic diseases can also cause hyperprolectinemia(4). Since, breast tissue has capability of local production of prolactin, thus rise in breast cancer could be local production with normal pituitary gland. There is an evidence of rise in prolactin levels in patients taking anti-psychotic drugs, which in turn causes rise in the rate of pre-cancerous lesions(5). On the other hand there is an evidence

that prolactin signaling pathway plays a role in breast cancer, thus paved a way for development of anti-prolactin anti-body(6). The prolactin receptor is reported to be over-expressed in breast cancers(7). However, prolactin pathway blockers couldn't show promising results in controlling disease progression in metastatic breast cancers. Previously reported studies have shown association of raised serum prolactin level with advanced and metastatic breast cancer(8).

Given the rise in breast cancer incidence in Pakistan and higher rate in younger patients it can be suspected that there are risk factors which need to be explored. From the available literature serum prolactin level in breast cancer in pre-menopausal women is least studied. Thus this study was conducted to describe range of serum prolactin in newly diagnosed breast cancer patients presenting with nipple discharge.

## METHODS

This was a descriptive cross-sectional study conducted from 20th July 2016 to 30th March 2022. During this period women under 50 years of age, diagnosed with breast cancer at the Department of Surgery, Indus Medical College, Tando Mohammad Khan, Pakistan were included. The study includes the women who presented with breast discharge with and without a clinically palpable lump in the breast. All these women had triple assessment for their discharge and serum prolactin levels were also assessed as a routine practice due to nipple discharge. These all patients were found to have a suspicious lump on ultrasound or mammogram and underwent biopsy to confirm the diagnosis of breast cancer. They all had MRI done to rule out Pituitary adenoma. Pregnant and lactating mothers were excluded. Women who were on any kind of medication were excluded. Women with pituitary adenoma on MRI were also excluded (n=3). The serum prolactin level was assessed from venous blood, within 4 hours of waking up by using Immunoassay. The reference range of the laboratory was followed and females having serum prolactin level >30 ng/ml were considered as having hyperprolactinemia. They all had normal liver function test, urea and creatinine.

Data was collected and analysed by using Statistical Package for Social Sciences version 28.0. Mean and standard deviation of the continuous variables were given. Categorical data has been presented as frequency distribution. Spearman correlation was applied to analyze association between age and serum prolactin levels.

## RESULTS

A total of 27 women presented with nipple discharge and normal brain MRI and underwent triple assessment to have a diagnosis of breast cancer. Mean age of the patients was 40 years (range 29 to 50 years ±SD 4.81). Five patients had a complaint of pain, 10 had discomfort and remaining (n=12) had no pain or discomfort. Great majority (n=22) had green or red blood discharge from nipple (Figure 1). Underlying breast lump was present in all patients. Nine patients did not complaint of any irregularity in their menstrual cycle and 15 patients reported delayed cycle.

Serum prolactin level was above normal reference range in all of these patients with mean levels at 276.67 (range 35.2- 570ng/ml, ±SD 163.93) ng/ml. There was no significant association of age and serum prolactin level found (p-value=0.57) (Figure 2).

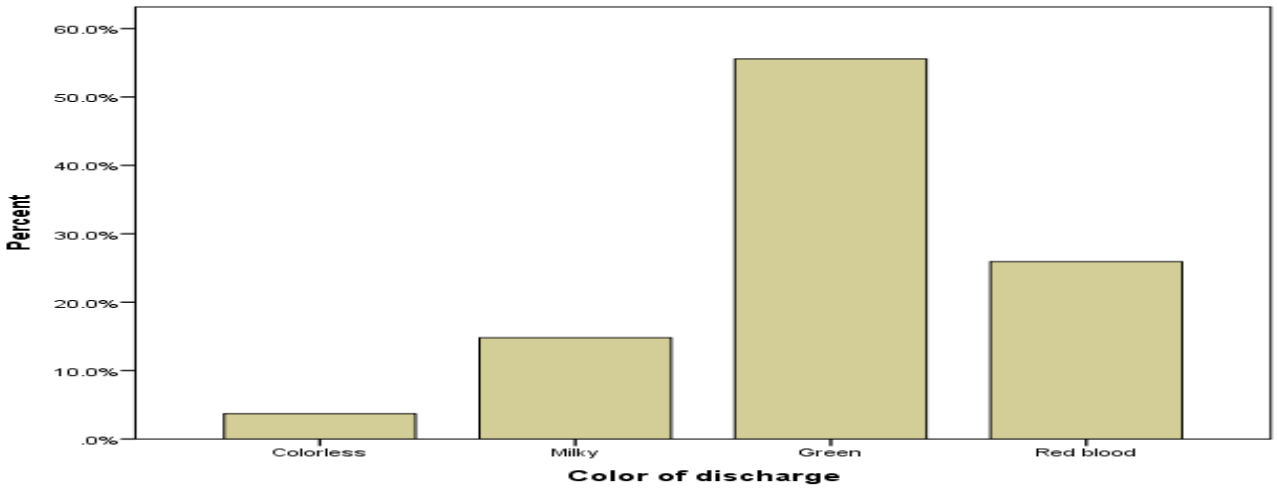


*Figure 1. Pattern of color of discharge in women having hyperprolactinemia*

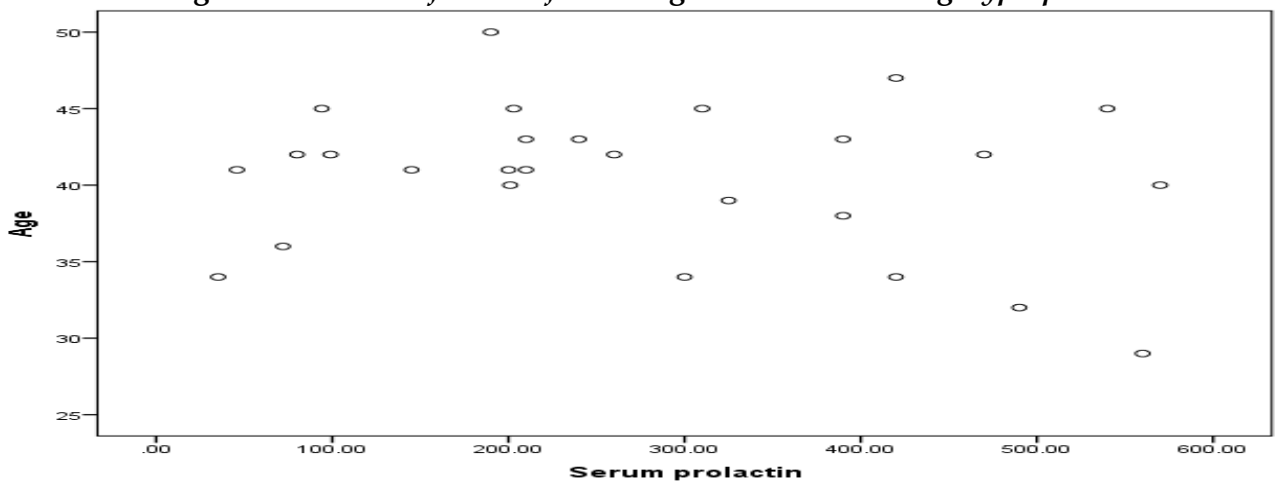


*Figure 2. Scatter plot presenting correlation of age and serum prolactin levels*

## DISCUSSION

The study has shown raised serum prolactin level in women presenting with nipple discharge without having any obvious reason of hyperprolactinemia in pre-manopausal women.

This is a complex pathway to understand as the raised prolactin is a cause of breast cancer or it's a feature. Both are equally possible. As there is evidence of local production of prolactin in breast tissue thus breast cancer might start producing more prolactin which in turn causes more progression thus a vicious circle of cancer cells and prolactin starts. However there is no evidence till date to comment on this theory. Though there is evidence available suggesting association of raised serum prolactin levels in women with advanced breast cancer(8).

On the other hand when it was reported to be associated with disease progression but the drugs (i.e. Raloxifene) which controlled other hormones did not affect prolactin in pre-manopausal women(9). Similar other studies have reported that prolactin is raised but not associated with disease specific clinical outcome neither it is associated with basic prognostic factors in breast cancer i.e. Oestrogen and progesteron. These findings were interestingly reported after 10 years long term in Naples Adjuvant (GUN) study(10). Another study was conducted to see the predictive significance of

prolactin in breast cancer and Bromocriptin was given but did not show any significant influence on disease outcome(11).

The high serum level of prolactin has been reported to be linked with resistance to chemotherapy in advanced breast cancer(12). With the same reference, it was thought that the use of a combination of chemotherapy with anti-prolactin therapy with be beneficial and improves response. But the studies have shown contradicting results. Some reported benefits of adding anti-prolactanemic therapy and others have shown no added benefit(11,13,14).

The study has a small sample size is considered as a limitation. However study from a single centre is the strength of the study.

## CONCLUSION

The study concludes that the younger women presenting with breast cancer has shown high serum prolactin level. The serum prolactin is an important novel factor can be added to breast cancer risk assessment and early detection system. Further large scale cohort studies are required to confirm these findings and established a role of serum prolactin in breast cancer.

## ETHICAL CONSIDERATION

The data was collected as part of the routine departmental data collection. Confidentiality of the patients was maintained.


## FUNDING

The study was conducted was part of routine data collection within the department, no additional funds required.


## REFERENCES


1. Bonneterre J, Peyrat JP, Beuscart R, Demaille A. Biological and clinical aspects of prolactin receptors (PRL-R) in human breast cancer. J Steroid Biochem Mol Biol [Internet]. 1990 Dec;37(6):977–81. Available from: https://linkinghub.elsevier.com/retrieve/pii/096007609090453R
2. GLOBOCAN 2020: New Global Cancer Data | UICC.
3. Vilar L, Vilar CF, Lyra R, Freitas M da C. Pitfalls in the Diagnostic Evaluation of Hyperprolactinemia. Neuroendocrinology [Internet]. 2019;109(1):7–19. Available from: https://www.karger.com/Article/FullText/499694
4. Thapa S, Bhusal K. Hyperprolactinemia [Internet]. StatPearls. 2022. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30726016
5. Rahman T, Patrick C, Ma C, Nicol GE, Reynolds CF, Mulsant BH, et al. Prolactin and Estrogen Levels in Postmenopausal Women Receiving Aripiprazole Augmentation Treatment for Depression. J Clin Psychopharmacol [Internet]. 2021 Jan;41(1):31–5. Available from: https://journals.lww.com/10.1097/JCP.0000000000001335
6. Agarwal N, Machiels J-P, Suárez C, Lewis N, Higgins M, Wisinski K, et al. Phase I Study of the Prolactin Receptor Antagonist LFA102 in Metastatic Breast and Castration-Resistant Prostate Cancer. Oncologist [Internet]. 2016 May 1;21(5):535-536i. Available from: https://academic.oup.com/oncolo/article/21/5/535/6401576

7. Costa R, Santa-Maria CA, Scholtens DM, Jain S, Flaum L, Gradishar WJ, et al. A pilot study of cabergoline for the treatment of metastatic breast cancer. Breast Cancer Res Treat [Internet]. 2017 Oct 3;165(3):585–92. Available from: http://link.springer.com/10.1007/s10549-017-4370-x
8. Mujagić Z, Mujagić H. Importance of serum prolactin determination in metastatic breast cancer patients. Croat Med J [Internet]. 2004 Apr;45(2):176–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15103755
9. Faupel-Badger JM, Prindiville SA, Venzon D, Vonderhaar BK, Zujewski JA, Eng-Wong J. Effects of Raloxifene on Circulating Prolactin and Estradiol Levels in Premenopausal Women at High Risk for Developing Breast Cancer. Cancer Epidemiol Biomarkers Prev [Internet]. 2006 Jun 1;15(6):1153–8. Available from: https://aacrjournals.org/cebp/article/15/6/1153/284580/Effects-of-Raloxifene-on-Circulating-Prolactin-and
10. De Placido S, Gallo C, Perrone F, Marinelli A, Pagliarulo C, Carlomagno C, et al. Prolactin receptor does not correlate with oestrogen and progesterone receptors in primary breast cancer and lacks prognostic significance. Ten year results of the Naples adjuvant (GUN) study. Br J Cancer [Internet]. 1990 Oct;62(4):643–6. Available from: http://www.nature.com/articles/bjc1990346
11. Peyrat J., Vennin P, Bonneterre J, Hecquet B, Vandewalle B, Kelly P., et al. Effect of bromocriptin treatment on prolactin and steroid receptor levels in human breast cancer. Eur J Cancer Clin Oncol [Internet]. 1984 Nov;20(11):1363–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/0277537984900543
12. Lissoni P, Vaghi M, Ardizzoia A, Fumagalli E, Tancini G, Gardani G, et al. Efficacy of monochemotherapy with docetaxel (taxotere) in relation to prolactin secretion in heavily pretreated metastatic breast cancer. Neuro Endocrinol Lett [Internet]. 2001;22(1):27–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11335876
13. Frontini L, Lissoni P, Vaghi M, Perego MS, Pescia S, Ardizzoia A, et al. Enhancement of the efficacy of weekly low-dose taxotere by the long acting anti-prolactinemic drug cabergoline in pretreated metastatic breast cancer. Anticancer Res [Internet]. 24(6):4223–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15736476
14. Fentiman IS, Chaudary MA, Wang DY, Brame K, Camplhjohn RS, Millis RR. PERIOPERATIVE BROMOCRIPTINE ADJUVANT TREATMENT FOR OPERABLE BREAST CANCER. Lancet [Internet]. 1988 Mar;331(8586):609–10. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673688914134

Research article

# HEMOSTATIC AND THROMBOTIC PARAMETERS IN ACUTE LEUKEMIA– A COMPARISON OF PRE AND POST REMISSION INDUCTION PHASE

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**ABSTRACT**

This study was aimed to compare hemostatic, fibrinolytic and thrombotic parameters in pre and post induction chemotherapy in acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL). A total of 110 diagnosed acute leukemia patients and 40 normal individuals were enrolled in the study. Questionnaire were filled and patients' blood specimens were collected before the commencement and post induction chemotherapy. Prothrombin time (PT), activated partial thromboplastin time (aPTT), von Willebrand factor antigen (vWF Ag), fibrinogen level, factor VIIIc (FVIIIc), D-Dimers, fibrinogen degradation products (FDPs), anti-thrombin III (AT), lupus anticoagulant (LA), protein C (PC), protein S and diluted russel viper venom test (DRVVT) were conducted in all the participants. A significant rise was identified in post-induction levels of PT, aPTT, vWF Ag, fibrinogen and factor VIII in acute leukemia patients. Analysis of fibrinolytic markers indicated increased D-Dimers and plasminogen levels while the levels of alpha 2 anti-plasmin were reduced in pretreated patients. Thrombotic markers' assessment showed increased levels of AT and LA while decreased level of PC in pretreated acute leukemia patients. It was concluded that remission induction chemotherapy, in acute leukemia patients, significantly affects the coagulation, fibrinolytic and thrombotic parameters.

**Key Words**: Hemostasis, Thrombotic markers , Fibrinolysis, pre and post induction chemotherapy, Leukemia

## INTRODUCTION

Impairment of hemostatic, fibrinolytic and thrombotic activities are frequently associated with hematological malignancies (1). Thrombosis was reported in patients with acute lymphoblastic leukemia on L-asparaginase therapy (2, 3). Thrombosis in these patients usually occurs as a result of disturbances in the anticoagulant and fibrinolytic systems (4). Hemostatic manifestations are not solely due to anticoagulant and fibrinolytic system disturbances; it is also associated with prolonged thrombocytopenia in these patients after the administration of chemotherapeutic drugs (5). It was noted that risk of bleeding was reduced in patients with acute leukemia receiving platelet transfusions

prophylactically and therapeutically (6). Acute promyelocytic leukemia is associated with life threatening condition of disseminated intravascular coagulation. Coagulopathy in APL has been studied extensively but several reports on ALL, especially in children, noticed that occurrence of DIC in adult ALL was 10% before treatment and 78% during remission induction therapy (7, 8).
Clinically non-significant bleeding manifestations were observed in patients with ALL (9). Primary activation of inflammatory mediators and proteases by severe infection, chemotherapeutic agents and secondary activation of fibrinolysis may play a role in compensation of activated coagulation in patients with leukemia (10). Formation of thrombin-antithrombin complex due to activation of prothrombin fragment 1+2 and as well as generation of thrombin increment produces pre-thrombotic state which can be identified by a thrombotic marker (F1+2) (11). Strandberg et al 2001 indicated von Willebrand factor defects in patients with acute leukemia (12). Leukemic cells produce procoagulants, plasminogen activators, proteinase in blood circulation resulting in proteolytic degradation of vWF (13). However, there is limited local data available on this aspect of acute leukemia. Identification of changes in hemostatic parameters in acute leukemia in pretreatment, post remission induction may help in reducing the morbidity and mortality rate by initiating early intervention for management of thrombosis and bleeding complications. Therefore, this study was designed to evaluate the hemostatic, fibrinolytic and thrombotic changes in patients with de novo AML and ALL prior to start of induction treatment and after the therapy.

## METHODS

The study was a observational study conducted at the Department of Biochemistry, University of Karachi, Pakistan and the Department of Hematology, National Institute of Blood Disease and Bone Marrow Transplantation (NIBD), Karachi, Pakistan from May 2011 to March 2012. Patients with confirmed diagnosis of acute leukemia were recruited into including Newly diagnosed and those in remission phase (n=110). A total of 40 age matched controls were included. Those with ambiguous diagnosis, history of hereditary bleeding disorder, or thromboembolic disease were excluded. Diagnosis of acute leukemia was established by a hemato-pathologist and verified by a panel of hematologists, according to the WHO classification. Study individuals were divided according to the following schema.

| | | |
|---|---|---|
| Controls | Age matched Control | n=40 |
| AML Day 0 | Newly diagnosed cases of acute myeloid leukemia | n=27 |
| AML Day 28 | Remission induction in acute myeloid leukemia | n=16 |
| ALL Day 0 | Newly diagnosed cases of acute lymphoblastic leukemia | n=38 |
| ALL Day 28 | Remission induction in acute lymphoblastic leukemia | n=29 |

### Laboratory methods

The hemostatic, fibrinolytic and thrombotic markers were analyzed at day 0 and 28 of treatment in patients as well as in controls. 65 patients including 27 of AML and 38 of ALL were newly diagnosed (at day 0) while 45 patients including 16 of AML and 29 of ALL received remission inductions. Six mL venous blood sample was collected from controls and patients at the time of diagnosis and at day 28 post chemotherapy. Blood sample was collected in 3.2% trisodium citrate with a ratio of 9:1. Platelet

free plasma was separated after centrifugation at 2000 x g for 20 minutes within 2 hours of blood collection and stored in blue coded cryo vials at -80°C till analysis.
Complete blood counts including platelet count were performed on automated hematology analyzer Sysmex XE-2100® (Sysmex Kobe, Japan). Peripheral blood smears were stained with Romanowsky's stain and observed under microscope.
Prothrombin time (PT), activated partial thromboplastin time (aPTT), quantitative determination of fibrinogen and determination of Factor VIII activity (FVIIIc) was done by clotting method. Quantitative determination of Von Willebrand factor antigen (vWF Ag), D-Dimers and free protein S (PS) was carried out by immunoturbidimetric method. Qualitative and semi-quantitative determination of fibrinogen degradation products (FDPs) was carried out by latex agglutination method. Determination of plasminogen, antiplasmin and Antithrombin III (AT) activity was performed by synthetic chromogenic substrate. Quantitative determination of functionally active protein C (PC) was done by chromogenic method. Screening of factor V Leiden was performed by coagulometric method based on modified aPTT with pre-dilution in factor V deficient plasma. Screening of lupus anticoagulant sensitive aPTT was conducted by clotting methods. Detection of lupus anticoagulant was carried out by simplified diluted Russel viper venom test (DRVVT) method in one stage clotting test.

### Statistical Methods

For quantitative analysis Mean±SD, minimum and maximum range, 95% confidence were calculated, while frequency and percentages were calculated for qualitative variables. Independent sample t-test was used to evaluate mean differences between control and cases of both types of acute leukemia. A p-value of $<0.05$ was considered significant.

## RESULTS

Total 110 diagnosed acute leukemia patients, including 75 males and 45 females were included in this study along with 40 healthy controls for comparison. Mean age of patients was 25.3±13.8 (range 1 to 65years).
Mean leukemic cell counts were high at day 0 as compared to day 28 patients while platelet counts were reduced at day 0 as compared to control group. However, leukemic cells decreased, and platelet count increased at day 28 than day 0. Mortality rate was higher in AML at day 28 than ALL whereas equal incidence of death was found in both type of leukemia at day 0 of treatment.
The hemostatic, fibrinolytic, and thrombotic markers were analyzed in plasma of AML and ALL patients at day 0 and 28 of treatment. Prothrombin time significantly increased in AML and ALL patients at day 0 as compared to control as well as in pretreated than treated cases of AML ($p<0.05$), whereas no difference was observed in case of ALL ($p>0.05$). The aPTT was significantly increased in AML and ALL at day 0 and 28 but no statistically significant difference found in between the both type of acute leukemia in pre and post treatment phases. Plasma levels of fibrinogen were higher as compared to controls in both types of acute leukemia in pre and post treatment phase($p<0.05$) while at day 28 markedly increased in AML and ALL as compared to day 0($<0.01$). Factor VIII level showing increased pattern at day 0 and 28 in both type of acute leukemia as compared to control ($p<0.01$). Von

Willebrand antigen levels were significantly higher in both phases of AML and ALL ($p<0.01$) whereas no difference was noticed in between at day 0 and 28 in cases of AML.

**Table 1. A summary of the comparison of controls and acute myeloid leukemia and acute lymphoid leukemia**

| Study population | | | | | |
|---|---|---|---|---|---|
| Variable | Healthy individuals | AML | | ALL | |
| Groups | C= 40 | NDM= 20 | RIM=16 | NDL=25 | RIL=25 |
| Age (years) | 29.5±4.5 (24-38) | 30.8±13 (15-65) | 29.0±18 (4-50) | 21.6 ± 11.1 (1– 38) | 19.9 ± 13.3 (1 – 59) |
| Male | 20 (50%) | 10 (50%) | 09 (56.2%) | 19 (76%) | 18(72%) |
| Female | 20 (50%) | 10 (50%) | 07 (43.7%) | 06(24%) | 07(28%) |
| Hb (g/dl) | 14.6±0.8 (12.4-16.7) | 9.1±1.7 (6.2-12) | 10.3±0.8 (9.2-11.9) | 9.2 ± 1.7 (5.9 – 12.7) | 10.7 ± 2.2 ( 7.6 – 16.1 ) |
| White Cells x109/L | 7.2±1.35 (4.5-11.8) | 48.6±40.6 (0.38-121.7) | 2.3±4.4 (0.2±16.8) | 48.6±40.6 (0.3-121.7) | 6.9 ± 7.6 (0.08 – 27.0 ) |
| Platelet x109/L | 255.7±43.1 (142-360) | 24.5±15.8 (3-59) | 76.2±72.7 (10-253) | 33.9 ± 38.9 (5-183) | 181 ± 156 ( 7- 573 ) |
| Blast % | NP | 72.5±32.6 (7-100) | 1.2±2.6 (0- 07) | 51.2 ± 29.6 ( 8 – 96 ) | 1.2±2.6 (0- 07) |

Markedly elevated levels of D-dimer in AML and ALL at day 0 and 28 compared to control($p<0.01$) was observed but showed significant reduction at day 0 in AML and ALL as compared to day 0 ($p<0.01$). Alpha 2 anti-plasmin significantly reduced as compared to control ($p<0.01$) in AML and ALL at day 0 but at day 28 significantly higher whereas no difference was observed in between day 0 and 28 of AML and ALL cases. Levels of Plasminogen were higher at day 28 but not significantly reduced as compared to controls.

Protein C significantly reduced in AML and ALL in both phases as compared to controls except in cases of ALL at day 28. Free protein S and factor V leiden did not show any significant association with acute leukemia. Antithrombin III was raised significantly in AML at day 0 and in ALL at day 28 although no statistical difference was observed in ALL. Lupus anticoagulant was higher in acute leukemia in both phases ($p<0.01$) while at day 28 more increased as compared to pretreatment which

was statistically significant ($p<0.01$). Findings in Table no.2 describes non overt DIC <5 score and overt DIC >5 in acute leukemia at day 0 and 28. Strong association of DIC was found in AML and ALL at day 0. Non overt DIC did not show any significant association with specific type of acute leukemia and it was equally expressed in both type of acute leukemia at day 0 and 28. (Table 2)
Frequency of gum bleeding (21%) and Bruises (12%) was observed marked in AML patients. Epistaxis (12%) was observed more in ALL patients.

**Table 2. DIC Score and association with leukemia's**

| | AML n(%) | | ALL n(%) | |
|---|---|---|---|---|
| **DIC Score** | **Day 0** | **Day 28** | **Day 0** | **Day 28** |
| < 5 | 15 (55.56%) | 16 (100%) | 30 (78.94%) | 27 (93.1%) |
| > 5 | 12 (44.44%) | 0 (0.0%) | 8 (21.06%) | 2 (6.9%) |

## DISCUSSION

The patients with acute leukemias are at high risk of both hemorrhage and thrombosis. Coagulation parameters have been studied and found that in both AML and ALL cases PT and APTT were significantly prolonged indicating coagulation factors derangement. Post chemotherapy results indicated the improvement of PT and APTT in AML while no significant results observed in ALL. Kwaan et al found that chemotherapy decreases the blast cell may be helpful in decreasing the PT, APTT levels. Chemotherapy L –asparginase is used to treat ALL patients, decreases the hepatic production in clotting factors, results no change of PT level was observed (14).
Cysteine proteinease is a cancer procoagulant is present in AML and ALL patients. This proteinase activates the factor X, increased generation of thrombi and utilized the coagulation factors, aggravate thrombotic complications. Increased production of thrombin by factor X, further acts to convert fibrinogen to fibrin and results prolonged PT and aPTT (15).
Acute liver failure is reported in course of acute leukemia which further affects the cascade of coagulation and deranged the clotting factors (16). Factors VIII demands vWF for transportation. Factors VIII and vWF was increased in AML and ALL patients. After chemotherapy, these factors reduced indicated as cancer cells decreased, they tend to decrease the factor VIII production by decreasing the procoagulants (17). The derangements of thrombotic markers were also observed in present investigation. Low level of protein C was found in AML and ALL pretreated patients. While increased Antithrombin III and Lupus was found significantly in both leukemias. This may predispose to venous thrombosis as described by Dixit and Troy (18, 19).
The investigation of fibrinolytic factors also showed the derangements in both leukemias. An increased generation of FDPSs was found due to an increases degradation of fibrin as described by Ketsueki et al. At day 28, both AML and ALL showed improved status of FDPSs.
While decreased plasminogen was observed in both pre and post treated leukemic patients. Ketsueki et al, was found in their investigation that in leukemic patients the tissue plasminogen activator level was increased which tends to convert the plasminogen into plasmin. This plasmin acts on fibrin and formed more FDPSs. Increased generation of plasmin increases cross linked fibrin that leads to the

formation of linked oligomers called D-Dimers. D-Dimers were also increased in patients with ALL and AML and decreased post chemotherapy due to the reduced formation of fibrin (20).
Alpha 2 antiplasmin usually binds with plasmin and inactivating it for downstream events. We investigated the increased level of alpha 2 antiplasmin in pre and post chemotherapy. Increased generation of plasmin is the evidence of increased consumption of plasminogen. And plasmin acts on fibrin to form FDPSs and nothing available to binds with A2AP, thus increases its level.
Lupus anticoagulant is serving as prothrombotic agent and initially is thought to be present in lupus erythematosus but now found to be present in leukemias as well. It is anti-lipid antibody and interferes both intrinsic and extrinsic coagulation cascades thus help in increasing the PT, aPTT level which is found in present investigation as well. Leukemic cells trigger the B cells to produce more antibodies abnormally, lupus anticoagulant is one of them. Leukemic cells via cytokines activate B cell to produced antiphospholipid antibodies including lupus anticoagulant. We also investigated the increased level of lupus anticoagulant in AML and ALL patients significantly (21).
Global parameters like platelet count, PT, fibrinogen and D-Dimer were used to score the level of DIC. FDPSs are valuable diagnostic tool for monitoring the DIC. Elevated level of FDPSs indicates the persistence of DIC while low level indicates decline of intravascular clotting.
At day 0 in patients with AML 44% cases had underlying overt DIC (>5.0) but 0% cases after induction of chemotherapy whereas in ALL no statistically significant difference was noted. This finding is consistent with other studies (23, 24).

## CONCLUSION

In conclusion, the leukemia patients are at high risk of bleeding, therefore supportive blood products should be administered, and serial laboratory monitoring of bleeding and thrombotic manifestations are required by using global hemostatic parameters in untreated patients, during and after the treatment. Early detection of thrombotic and hemostatic defects and active intervention will help in reducing the morbidity and mortality due to hemorrhage and thrombotic complications and provide better survival with good quality of life.

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## CONFLICT OF INTEREST

Authors declare no conflict of interest.

## ETHICAL CONSIDERATION

For ethical issue, all participants and their legal guardians gave informed consent, and their confidentiality and anonymity were protected.

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## REFERENCES


1. Speiser W, Pabinger-Fasching I, Kyrle PA, Kapiotis S, Kottas-Heldenberg A, Bettelheim P, Lechner K. Hemostatic and fibrinolytic parameters in patients with acute myeloid leukemia; Activation of blood coagulation, fibrinolysis and unspecific proteolysis. Blut 1990; **61**: 298-302.
2. Frantzeskaki F, Rizos M, Papathanassiou M, Nikitas N, Lerikou M, Armaganidis A, Dimopoulos G. Am J Case Rep. 2013 Aug 14;14:311-4.
3. Hongo T, Okada S, Ohzeki T, Ohta H, Nishimura S, Hamamoto K, Yagi K, Misu H, EguchiN, Suzuki N, Horibe K, Ueda K. Low plasma levels of hemostatic proteins during the induction phase in children with acute lymphoblastic leukemia: A retrospective study by the JACLS. Japan Association of Childhood Leukemia Study. Pediatr Int 2002; **44**: 293- 9.
4. Toft N, Birgens H, Abrahamsson J, Griskevicius L, Hallbook H, Heyman M, Klausen TW, Jonsson OG, Palk K, Pruunsild K, Quist-Paulsen P, Vaitkeviciene G, Vettenranta K, Asberg A, Helt LR, Frandsen T, Schmiegelow K. Eur J Haematol. 2016;96(2):160-9.
5. Webert K, Cook RJ, Sigouin CS, Rebulla P, Heddle NM. The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia. Haematologica 2006; **91**: 1530-7.
6. Dayama A, Dass J, Seth T, Mahapatra M, Mishra PC, Saxena R. Indian J Cancer. 2015 Jul-Sep;52(3):309-12.
7. Tallman MS, Kwaan HC. Reassessing the hemostatic disorder associated with acute promyelocytic leukemia. Blood 1992; **79**: 543- 53.
8. Solano C, López J, Gómez N, Fernandez-Rañada JM. Acute lymphoblastic leukemia: hypofibrinogenemia with a low incidence of clinical complications is often found during induction remission therapy. Blood 1992; **80**:1366-8.
9. Sarris A, Cortes J, Kantarjian H, Pierce S, Smith T, Keating M, Koller C, Kornblau S, O'Brien S, Andreeff M. Disseminated intravascular coagulation in adult acute lymphoblastic leukemia: frequent complications with fibrinogen levels less than 100 mg/dl. Leuk Lymphoma 1996; **21**: 85-92.
10. Martí-Carvajal AJ, Anand V, Sola I. The Cochrane database of systematic reviews. 2015 24;6:
11. Brummel-Ziedins KE, Vossen CY, Butenas S, Mann KG, Rosendaal FR. Thrombin generation profiles in deep venous thrombosis. J Thromb Haemost 2005; **3**: 2497-505.
12. Strandberg K, Bhiladvala P, Holm J, Stenflo J. A new method to measure plasma levels of activated protein C in complex with protein C inhibitor in patients with acute coronary syndromes. Blood Coag Fibrinolysis 2001; **12**: 503-10.
13. Federici AB, D'Amico EA. The role of von Willebrand factor in the hemostatic defect of acute promyelocytic leukemia. Leuk Lymphoma 1998; **31**: 491-9.
14. Kwaan HC. Double hazard of thrombophilia and bleeding in leukemia. Hematol Am Soc Hematol Educ Prog 2007:151-7.
15. Zaki S, Burney IA, Khurshid M. Acute Myeloid Leukemia in Children in Pakistan. J Pak Med Assoc 2002; **52**: 247-9.
16. Cesur S, Topuoulu P, Apik O, Burengel S, Zcan M. Acute Hepatic Failure in a Case of Acute Lymphoblastic Leukemia. Turk J Med Sci 2004; **34**: 275-9.

17. Klingemann HG, Kosukavak M, Höfeler H, Havemann K, Hoppe Seylers Z. Fibronectin and factor VIII-related antigen in acute leukaemia. Physiol Chem 1983; **364**: 269-77.
18. Dixit A, Kannan M, Mahapatra M, Choudhry VP, Saxena R. Roles of protein C, protein S, and antithrombin III in acute leukemia. Am J Hematol 2006; **81**: 171-4.
19. Troy K, Essex D, Rand J, Lema M, Cuttner J. Protein C and S levels in acute leukemia. Am J Hematol 1991; **37**: 160.
20. Ketsueki R. Persistent discrepancy between FDPS and D-dimer in a patient with acute leukemia. Rinsho Ketsueki 1995; **36**: 212-7.
21. Ediriwickrema LS, Zaheer W. Diffuse Large Cell Lymphoma Presenting as a Sacral Mass and Lupus Anticoagulant. Yale J Biol Med 2011; **84**: 433- 8.
22. Toh CH, Hoots WK. The scoring system of the Scientific and Standardisation Committee on Disseminated Intravascular Coagulation of the International Society on Thrombosis and Haemostasis: a 5-year overview. J Thromb Haemost 2007; **5**: 604-6.
23. Falanga A, Rickles FR. Pathogenesis and management of the bleeding diathesis in acute promyelocyticleukaemia. Best Pract Res Clin Haematol 2003; **16**: 463-82.
24. Wilde JT, Kitchen S, Kinsey S, Greaves M, Preston FE. Plasma D-dimer levels and their relationship to serum fibrinogen/fibrin degradation products in hypercoagulable states. Br J Haematol 1989; **71**: 65-70.

*Research article*

# NIGHT TIME SPLINTING WITHOUT SURGERY FOR DUPUYTREN'S CONTRACTURE – A SUCCESSFUL CASE SERIES OF ELDERLY PATIENTS FROM A SINGLE CENTER

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**ABSTRACT**

Dupuytren's contracture is a musculoskeletal deformity mainly involves fingers of the hands. Elderly diabetic patients more frequently suffer from the problem. Currently available options of treatment include needling, clostridium histolyticum injection and surgery. Following surgery patients are supposed to apply splint to correct the contracture. This study was conducted on early stage contracture, including 18 patients. All were advised to massage the area of contracture in the morning and at night following by application of splint at night time. 16 patients showed complete recovery with average duration of 3.5 weeks. None of them has recurrence after three weeks of follow-up. The study concludes that the early stage contracture can be successfully treated by conservative measures.

**Key Words**: Dupuytren's Contracture, Elderly diabetics, Hand deformity

## INTRODUCTION

Dupuytren's Contracture is a musculoskeletal deformity affecting hands. Most commonly involving ring and little fingers(1). The contracture occurs in the palmer tendons causing contracture with presence of thickening and nodule(2). It does not cause pain and it is reported to be slow progressive. Since it commonly involves ring and little fingers thus it does not cause a major deformity and patients continue to do their routine chores. The disease risk increases with advancing age and has significant association with diabetes. As reported the incidence under 50 years is around 7% which approaches 40% at the age of 70 years(3).

It is clinically diagnosed on examination of the affected hand, where there is a nodule in the ligament causing contracture of the fingers(4). The treatment currently offered includes needling, where cord is punctured with the help of needle, enzyme injection with collagenase i.e. Clostridium Histolyticum to break the cord, then there is option of surgery(5). All of these are invasive options, thus patients had to wait to develop the disease at the stage where they accept invasive procedures. The patients coming at initial stage (without fixed contracture) of the disease are left with just management of the hand with physical therapy without any scientific evidence of its effectiveness.

On the other hand with ageing population and improvement in health care facilities with development of orthopedic sub-specialty more people are coming with early disease where there is still need for non-invasive procedures and needling and surgery is not justified. Therefore a pilot study was conducted on three patients initially where they were advised to have massage of warm oil and bed time splint application on the affected fingers. These patients showed complete reversal of the problem and the nodule dissolved.

Based on these preliminary findings this prospective study was conducted to see the effectiveness of bed time splinting to cure initial stage dupuytren's contracture in elderly diabetic population.

## METHODS

This is a prospective experimental study including 18 patients with early stage dupuytren's contracture. The patients included were over 60 years of age with diabetes. The early stage dupuytren's contracture was defined as deformity which has not become fixed, patient can straighten fingers with pressure, and there was no pain. Figure 1 shows hand of an elderly women presented with contracture and included in this study. They presented to the Sindh employees Social Security Institution, Hyderabad during the period between January 2015 and December 2021.

They all were advised to have massage, mainly putting pressure (mild to moderate) on the site of the nodule, twice a day with warm oil. At night after massage they were advised to apply metal extension splint. They were asked to remove the splint in the morning, and massage as soon as the splint was removed. Patients were followed up for two months on weekly basis.

The data was collected on SPSS version 22. The time of the success of therapy was evaluated in weeks. The results were analysed as frequency distribution for categorical variables and mean and standard deviation for continuous variables.

**Figure 1. Image of Dupuytren's contracture in a female diabetic patient having ring finger contracture (Image presented with permission and signed consent of the patient).**

## RESULTS

There were 18 patients presented with early stage dupuytyren's contracture. Mean age of the patients was 66.83 years (range 61- 77, ±SD =5.03). There were 12 females and 6 males. Majority of the patients noticed the contracture within three months. Initially was on and off and more recently it become

constant. However they were able to straighten with pressure. Ten patients ring finger involved, 2 had little finger and 6 had both ring and little fingers involved.
Out of these patients 16 (88.9%) had reversed the contracture, while two patients required needling. Mean duration of the successful recovery was 3.5 weeks (range 2-5 weeks). There was no recurrence reported after three months.

## DISCUSSION

The study showed almost 90% success rate of non-invasive method of reversal of early stage dupuytren's contracture in elderly diabetic population. The response to non invasive therapy was remarkable without any recurrence at short term.
The dupuytren's contracture is a fibroproliferative disease, commonly seen in the elderly people and diabetes is one of its risk factors(6). The treatment has options with needle injections, and surgery. All are reported to be associated with varying degree of complications(7). Though percutaneous needle fasciotomy reported to be the safest and well tolerated but procedure is invasive in nature and reportedly 86% of recurrence with procedure repeated(7). The Clostridium histolyticum treatment was associated with skin tearing in 11% of patients undergoing treatment had skin tearing(8). The risk of recurrence and repeated procedure was high with required repeated procedure or surgery within 6 weeks(9). Though there is evidence of good response for `4-weeks intervention and maintenance of the response for more than 12 weeks has also been reported in studies exploring efficacy of Clostridium histolyticum(10). Another study which used collagenase injection followed by finger exercise and splint wearing at night showed promising results(10). However with this treatment bruising and edema was the most frequently observed complications(11).
There was a randomized controlled trial DupuytrEn Treatment EffeCtiveness Trial (EFFECT) comparing three arms of treatment including clostridium histolyticum injection and limited fasciectomy in non-responsive cases, percutaneous needle fasciotomy and primary limited fasciotomy. The trail was planned and approved in 2018 and followed of 10 years is awaited(12).
The study has small sample size and the selection criteria based on clinical assessment only. Thus we consider this as a limitation. However the study opens up an era of first line conservative management for dupuytren's contracture.

## CONCLUSION

This small scale prospective study presented high rate of success of massage with night time extension splint application with 88% cure rate. There was no recurrence during the period of study. Further large scale randomized controlled trials are recommended for robust clinical guidelines.

## ETHICAL CONSIDERATION

This was an institutional study approved by local ethics committee, all patients signed and informed consent.

## CONFLICT OF INTEREST

Authors declare no conflict of interest

## FUNDING

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## REFERENCES


1. Benson LS, Williams CS, Kahle M. Dupuytren's Contracture. J Am Acad Orthop Surg. 1998;6(1).
2. Trojian TH, Chu SM. Dupuytren's Disease: Diagnosis and Treatment. Am Fam Physician. 2007;76(1):86–9.
3. Gudmundsson KG, Arngrímsson R, Sigfússon N, Björnsson Á, Jónsson T. Epidemiology of Dupuytren's disease. J Clin Epidemiol [Internet]. 2000 Mar;53(3):291–6. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0895435699001456
4. Woodruff MJ, Waldram MA. A Clinical Grading System for Dupuytren's Contracture. J Hand Surg Am [Internet]. 1998 Jun 29;23(3):303–5. Available from: http://journals.sagepub.com/doi/10.1016/S0266-7681%2898%2980045-4
5. Yoon AP, Kane RL, Hutton DW, Chung KC. Cost-effectiveness of Recurrent Dupuytren Contracture Treatment. JAMA Netw open [Internet]. 2020;3(10):e2019861. Available from: http://www.ncbi.nlm.nih.gov/pubmed/33030553
6. Samulėnas G, Rimdeika R, Braziulis K, Fomkinas M, Paškevičius R. Dupuytren's Contracture: Incidence of Injury-Induced Cases and Specific Clinical Expression. Medicina (Kaunas) [Internet]. 2020 Jun 30;56(7). Available from: http://www.ncbi.nlm.nih.gov/pubmed/32629785
7. Moog P, Buchner L, Cerny MK, Schmauss D, Megerle K, Erne H. Analysis of recurrence and complications after percutaneous needle fasciotomy in Dupuytren's disease. Arch Orthop Trauma Surg [Internet]. 2019 Oct;139(10):1471–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31367843
8. Zhang D, Blazar P, Benavent KA, Earp BE. Long-term Effects of Skin Tearing on Outcomes After Collagenase Treatment of Dupuytren Contractures. Hand (N Y) [Internet]. 2021;16(6):792–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31941375
9. Nayar SK, Pfisterer D, Ingari J V. Collagenase Clostridium Histolyticum Injection for Dupuytren Contracture: 2-Year Follow-up. Clin Orthop Surg [Internet]. 2019 Sep;11(3):332–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31475055
10. Sakai A, Zenke Y, Menuki K, Yamanaka Y, Tajima T, Tsukamoto M, et al. Short-term efficacy and safety of collagenase injection for Dupuytren's contracture: Therapy protocol for successful outcomes in a clinical setting. J Orthop Sci [Internet]. 2019 May;24(3):434–40. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30392714
11. Fei TT, Chernoff E, Monacco NA, Komatsu DE, Muhlrad S, Sampson SP, et al. Collagenase Clostridium histolyticum for the Treatment of Distal Interphalangeal Joint Contractures in Dupuytren Disease. J Hand Surg Am [Internet]. 2019 May;44(5):417.e1-417.e4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30146387
12. Räisänen MP, Karjalainen T, Göransson H, Reito A, Kautiainen H, Malmivaara A, et al. DupuytrEn Treatment EffeCtiveness Trial (DETECT): a protocol for prospective, randomised, controlled, outcome assessor-blinded, three-armed parallel 1:1:1, multicentre trial comparing the effectiveness and cost of collagenase clostridium histolyticum, per. BMJ Open [Internet]. 2018;8(3):e019054. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29599391

Research article

# ASSESSMENT OF MACULAR FUNCTION IN DENSE CATARACT USING BY MADDOX ROD

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**ABSTRACT**
Cataract is a leading cause of blindness worldwide. However there is surgical option available for treatment with complete cure in majority of patients. For dense cataract Maddox Rod was evaluated. A total of 200 patients were recruited. Maddox Rod test for macular function appears to be useful in a great majority of patients. The assessment of macular function in dense cataract is difficult but the Psycho physiological test like Maddox rod test was found to be the reliable in patients with cataract and its quick and understandable

**Key Words**: Cataract, macular function test, Maddox rod assessment.

## INTRODUCTION

Cataract is the prominent cause of vision loss globally, resulting in 47.8% (equals to 17.7 million) people blind (1). The survey was conducted to explore prevalence of blindness and reported to have 570 000 blind adults in Pakistan due to cataract, additional 3560000 eyes have reduced visual acuity at <6/60 as a result of cataract. Though the surgical management is now hallmark of treatment with complete reversal of vision but there are people who develop mature cataract and some present with hypermature due less privileged population with inadequate health care facilities (2). As reported in the literature that 253 million people around the globe are living with some degree of vision loss, out of which 36 million have complete vision loss to the degree of blindness and remaining 217 million with varying degree of impairment ranging from moderate to severe vision impairment. A demographic study report suggested that 81% of blind people or patients with varying degree of vision impairment are aged 50 years or older. Primary cause of vision impairment globally is chronic eye diseases. Untreated cataract and refractive errors which left untreated are most commonly reported causes of vision loss worldwide. However in developing and low-middle income countries untreated cataract remains at the top(3).

The macula is a pigmented area, oval in shape presented in human eye adjacent to the center of the retina. In human's eye macula measures around 5.5 mm (0.22 in) in diameter. It is mainly responsible for the central, high-resolution, color vision in good light. If the macula is damaged this kind of high resolution light vision is impaired, such condition include macular degeneration(4). The diagnosis and treatment outcome measurement in cases of macular diseases Macular function tests

are needed. This tests is also required for the evaluation of the macular function with opaque media in conditions including dense cataract and vitreous hemorrhage. Dense cataract is a challenge for assessment of macular function. There is limited information regarding Maddox rod is available for utilization in dense cataract. Thus we have designed this study to evaluate the response of macular function in patients presenting with dense cataract by using Maddox rod.

## METHODS

This was hospital based cross-sectional, observational study. Patients were selected by using a non-probability convenient sampling method, where all the patients without any gender restriction coming to Out Patient Department of Al-Ibrahim Eye Hospital, Karachi, Pakistan were included. The study was conducted between May 2019 to October 2019. The patients included were presenting with dense cataract and above 30 years of age. Their visual acuity must be ≤ 6/60-1/60, with no fundus glow and consented to be part of the study.

**Maddox Rod Test method**

All patients were asked to sit approximately 1 foot away (33 cm) from a bright light source and Maddox rod was placed in front of the eye planned to be examined. Patient was asked to close the other eye. The Maddox rod was rotated in two peaks in vertical and horizontal directions. Patients were asked to see in a line, look at its color, focus on the continuity, the direction of the line and straightness it shows. The results were then graded as per standard protocol.

**Statistical Methods**

Statistical package for social sciences (SPSS) version 20.0 was used for data collection and analysis in our project. Mean and standard deviation were considered for continuous variables while the categorical variables were presented as frequency distribution.

## RESULTS

Out of 200 patients selected for this study there were 156 (78%) females and 44 (22%) males. Mean age of the participants was 57.02 ± 9.0 years (range 38- 85 ±SD=9.011). The visual acuity of 62 (31.0%) patients was 1/60, 53(26.5%) had 6/60, 41(20.5%) had 3/60, 35(17.5%) had 2/60 and 9(4.5%) had 5/60. Out of 200 patients 164 (82.0%) had shown a Grade 1 response, 22 (11.0%) had shown Grade 2 response, 9 (4.5%) had shown Grade 3 response and 5 (2.5%) had shown Grade 4 response with Maddox rod (Figure 1). The grading of Maddox rod according to Visual Acuity is presented in Table 1.

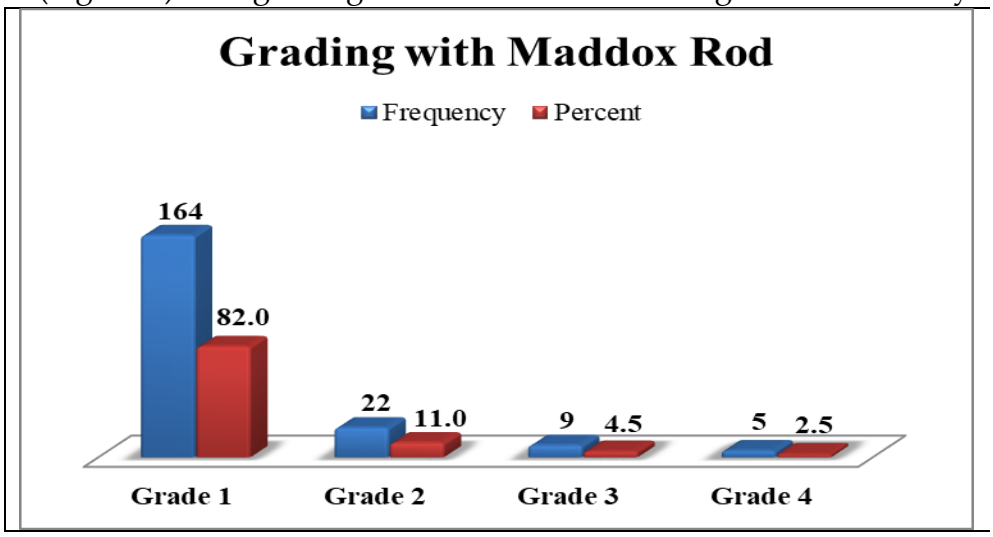


**Figure 1. Pattern of distribution of Grading with Maddox Rod**

**Table 1. Frequency distribution of Visual Acuity according to Grading with Maddox rod**

| Grading with Maddox rod | Visual Acuity | | | | | Total |
|---|---|---|---|---|---|---|
| | 6/60 | 5/60 | 3/60 | 2/60 | 1/60 | |
| Grade 1 | 51 | 8 | 33 | 28 | 44 | 164 |
| Grade 2 | 1 | 0 | 6 | 6 | 9 | 22 |
| Grade 3 | 1 | 1 | 2 | 1 | 4 | 9 |
| Grade 4 | 0 | 0 | 0 | 0 | 5 | 5 |
| **Total** | 53 | 9 | 41 | 35 | 62 | 200 |

## DISCUSSION

In this study total of two hundred patients attended OPD during the data collection period. The Maddox rod test appeared reasonable in making a diagnosis in dense cataract cases. It was recognized as a preferable clinical test to assess the functioning of macula prior to cataract surgery. However, there were only 5 patients where the test did not appear to be useful which makes 2.5% only.

The previously reported cases have shown that Maddox rod test is a reliable pre-clinical assessment test before cataract surgery in addition to the clinical examination, visual acuity and ophthalmologic ultrasound(5). There is a wide variation in the ophthalmologists practice in the preference of tests being used in clinical practice. A national survey from St. Lious reported in 1995, and showed that a considerable number of ophthalmologists did not perform such tests to make a firm diagnosis(6).

In this study 164 (82.0%) patients given Grade 1 response 22 (11.0%) had shown Grade 2 response, 9 (4.5%) had shown Grade 3 response and 5 (2.5%) had shown Grade 4 response with Maddox rod. which give a sign that they had potential visual acuity behind the cataract. On the other hand a study of conventional macular function test in cases of cataract was conducted in the Rotary eye hospital in Gujarat, India, out of operated 100 cases 80% achieved a visual acuity of 6/6 to 6/9 post surgically (7). These patients had Grade I response on Maddox rod test. In these reported cases four had grade II response to Maddox rod test. A total of six patients gained a visual acuity of 6/24 to 6/36, five of these cases were categorized as Maddox rod response grade III, and one was reported to have a grade I response. There has been reported variations in the interpretation of the ophthalmic reports between clinician(8). According to the previous study they performed the Maddox rod test after cataract surgery and in this study the Maddox rod test performed before cataract surgery.

The answer to my question I finally found that the most common response in this study was Grade 1 with Maddox rod in 164(82.0%) amongst the total 200(100%) patients with dense cataract of 200 eyes, which gives the sign that the macula was functioning and the visual potentials were present behind the cataract.

The limitations to the study were that the limited time duration, sample size and the category of visual acuity in patients with dense cataract. The macular diseases which inhibit the grading of Maddox rod

in some patients, was not documented in this study and the follow up results must be checked with Maddox rod after the surgery. The recommendations to the study were to assess the macular functioning by Psycho physiological test; Maddox rod in opaque media if other devices like B-scan are not available, it is helpful in the assessment whether the macula is functioning or not, and the cataract surgery will reliable in any severe condition.

## CONCLUSION

The assessment of macular function in dense cataract is difficult but the Psycho physiological test like Maddox rod test was found to be the reliable in patients with cataract and its quick and understandable.

## CONFLICT OF INTEREST

Authors declare no conflict of interest.

## ETHICAL CONSIDERATION

The study was approved by local ethical committee


## FUNDING

The study was conducted from Departments own resources no additional funds required.


## REFERENCES


1. Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, et al. Global data on visual impairment in the year 2002. Bull World Health Organ [Internet]. 2004 Nov;82(11):844–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15640920
2. Jadoon Z, Shah SP, Bourne R, Dineen B, Khan MA, Gilbert CE, et al. Cataract prevalence, cataract surgical coverage and barriers to uptake of cataract surgical services in Pakistan: the Pakistan National Blindness and Visual Impairment Survey. Br J Ophthalmol [Internet]. 2007 Oct 1;91(10):1269–73. Available from: https://bjo.bmj.com/lookup/doi/10.1136/bjo.2006.106914
3. Steinmetz JD, Bourne RRA, Briant PS, Flaxman SR, Taylor HRB, Jonas JB, et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. Lancet Glob Heal [Internet]. 2021 Feb;9(2):e144–60. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2214109X20304897
4. Choi CJ, Melki SA. Maddox rod effect to confirm the visual significance of laser in situ keratomileusis flap striae. J Cataract Refract Surg [Internet]. 2011 Oct;37(10):1748–50. Available from: https://journals.lww.com/02158034-201110000-00003
5. Thurschwell LM. Presurgical evaluation of patients with cataracts. Optom Clin [Internet]. 1991;1(2):159–87. Available from: http://www.ncbi.nlm.nih.gov/pubmed/1799825
6. Bass EB. Variation in Ophthalmic Testing Prior to Cataract Surgery. Arch Ophthalmol [Internet]. 1995 Jan 1;113(1):27. Available from: http://archopht.jamanetwork.com/article.aspx?doi=10.1001/archopht.1995.01100010029018

7. Dubey AK, Masani PH, Shroff AP. Quantitative assessment of conventional macular function tests in cases of cataract. Indian J Ophthalmol [Internet]. 1983;31 Suppl:895–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/6544281
8. Steinberg EP. Variation in Ophthalmic Testing Before Cataract Surgery. Arch Ophthalmol [Internet]. 1994 Jul 1;112(7):896. Available from: http://archopht.jamanetwork.com/article.aspx?doi=10.1001/archopht.1994.01090190044020

Research article

# ANALYSIS OF PATTERN OF ABO BLOOD GROUPS IN PEDIATRIC DIABETIC PATIENTS – AN OBSERVATIONAL STUDY

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**ABSTRACT**

Diabetes Mellitus (DM) is the most frequently occurring metabolic disorder, caused by inadequacy in secretion of insulin or malfunction leading to chronic hyperglycemia. Well-established corroborations have been reported in the literature suggesting association of ABO blood group with DM. The available literature focuses on adult population, with limited information of said association in children. Thus this study was aimed to determine the association of ABO blood group with Diabetes in pediatric patients having confirmed diagnosis. This was a comparative cross sectional study conducted from October 2021-January 2022 at Endocrinology Ward, Children Hospital Lahore (CHL), Pakistan. The study was approved by the local research ethics committee of CHL and conducted according to the declaration of Helsinki 2000. Blood grouping was done by forward and reverse methods. A total of 25 patients, including 18 males and 7 females were included. Frequency of blood group B (n=10;40%) was highest followed by blood group O (n=4;16%), A blood group (n=3;12%), and AB (n=1;4%) in males. In females, the blood group AB (n=3;12%) has the highest frequency followed by O (n=2;8%). Blood group A (n=1;4%) and B (n=1;4%) had the same frequency among female diabetic patients.

**Key Words**: Diabetes mellitus, ABO blood groups, Endocrinology, Type I Diabetes, Pediatric age group.

## INTRODUCTION

Diabetes mellitus (DM) is a chronic disorder characterized by hyperglycemias as a result of insulin dysfunction or reduced release or development of insulin resistance at cellular level. Diabetes mellitus may occur due to disturbed metabolism of carbohydrates, protein and fat which as a result of deficiency in insulin secretion or insulin malfunction or in combination (1). Pathogenesis of diabetes mellitus has a very wide range from pancreatic cell destruction due to autoimmune disorder (2). Diabetes Mellitus is comprised of two types including insulin-dependent diabetes mellitus (IDDM or Type I), which results from the reduced insulin production, and non-insulin-dependent diabetes mellitus (NIDDM or type 2) related to the insulin resistance at the peripheral level, where insulin level remains normal or sometimes even enhanced but unable to maintain blood glucose levels (3). In Type

1 diabetes mellitus the insulin-making cells in the pancreas are destroyed by the immune system. The cell of the pancreas which produce insulin are called beta cells (4). This type of diabetes mellitus is more common in children and young people so it has another name called juvenile diabetes mellitus (5).

Type 2 DM is the most frequently reported type accounting for ~95% of all diabetic cases (6). While DM type I is commonly seen in pediatric population. On the other hand blood grouping is determined by the presence of genetic pattern inherited from mother and father. There are two fundamental systems used for blood grouping, that is ABO system based on A and B antigen i.e. A blood group: having A antigen on Red blood cells (RBC), B blood group suggest B antigen on RBC, AB blood group having both A and B antigen while O blood group have none. It is interesting that the blood group having A antigen will have anti-B antibodies and vice versa. The Rh grouping determines the presence of Rh antigen and divides each blood group of ABO system into two groups; positive and negative.

Blood grouping is a genetic determination, thus there is some disease preponderance, where some diseases are found more in one blood group than the other. Given the nature of DM in children this study was conducted to evaluated the pattern of ABO blood grouping pediatric children.

## METHODS

This was a comparative cross-sectional study, conducted from October 2021 to January 2022 at endocrinology ward, Children Hospital Lahore (CHL), Pakistan. The study was approved by the ethical committee of CHL and performed according to the declaration of Helsinki 2000. Total 25 diagnosed cases of diabetes mellitus and same number for healthy (non diabetic) controls with age range 1 to 18years were included. The samples were collected through convenient sampling from the endocrinology ward of Children Hospital Lahore. For assessment of blood group whole blood was drawn in an EDTA vial (Lavender top) and a heparinized serum vial (Yellow top). Both forward and reverse grouping was performed in the blood bank following standard procedure (7).

Statistical package for the social sciences (SPSS) version 23 was used for the analysis of the data. Frequencies were evaluated and Chi-square test was used for the association between variables. A p-value was set at 0.05, and <0.05 was considered significant.

## RESULTS

Total 25 patients and equal number of healthy controls' samples were analyzed including 7 females in the study group and 18 males, while in control group 16 were males and 9 were females. The blood group B (n=11; 44%) followed by blood group O (n=6; 24%) were high in patients with diabetes mellitus. While blood group A and AB were shown to have equal frequencies (n=4; 16%). Among the healthy controls, the frequency of blood group B (11; 44%) was the highest followed by blood group A (9; 36%) and O (5; 20%). The least frequency among all the healthy control showed by blood group AB (0; 0%), as shown in Table 1. There was a significant difference in the distribution of A and O groups (p-value <0.001).

**Table 1. Comparison of ABO blood groups in Diabetic pediatric patients and healthy controls**

| Blood group | Controls n(%) | Cases n(%) | p-value |
|---|---|---|---|
| A | 9(36) | 4(16) | <0.001 |
| B | 11(44) | 11(44) | 0.42 |
| AB | 0 | 4(16) | 0.09 |
| O | 5(20) | 6(24) | <0.001 |

## DISCUSSION

Populations showing genetic association with diabetes mellitus are crossbreed populations comprised of the recent parenteral populations mixing in addition to the ancestral mixing. The available literature has conflicting data regarding association of blood grouping and DM, showing positive association in some studies and no significant in others. B blood group has shown more association among all blood groups.

The study on the association of the ABO blood group with diabetes mellitus in Bangladesh shows that there is no significant association between blood group distribution and diabetes mellitus, in which they studied 2,312 patient samples and 8,936 control samples (8). On the contrary, this study has shown the frequency of blood group B is highest among all, and O and AB blood groups are least. Further investigation and confirmation of my studies can be done by using a larger sample size.

In India, the study on the association of the ABO blood group has also been carried out on 511 patients with different racial distribution and 475 healthy control samples from the same geographical and socioeconomic status with the patients provided the exclusion of diseased condition (9). Another research study demonstrated that the frequency of A and O blood group is higher in healthy controls than in diabetic patients but statistical significance was still absent. For controls, the statistical significance was present in terms of racial distribution but still absent in diabetic patients (10). In current study, the prevalent blood group was B (44%) both among diabetic patients and healthy controls even having the same frequencies but there was no statistical significance p-value <0.05. AB blood group had the least frequency both in patients and healthy controls. However, the blood group A and O have shown lower frequencies among diabetic patients 16% and 24% respectively, and the same for AB which might be protective against DM. In this study the association of gender and blood groups of both patients and control samples have also been studied, which shown a significant association in chi-square test. The frequency of male (18;72%) among 25 diabetic patients is higher than females (7;28%) so, male are at higher risk of acquiring diabetes mellitus then females. Further, among males, those having blood group B (10;40%) are at risk because its frequency is highest among all others. Among female patients AB blood group has highest percentage (3;12%) so, in females the AB blood group is at higher risk than others. In normal control sample the frequency of male (16;64%) is higher than female (9;36%) but still lower than in patients which is 72%. These results confirm the higher association of male with diabetes mellitus. However, due to limitations of time and resources and small sample size this study has not been conducted at broader level. Further investigation on this association should be done.

## CONCLUSION

The results obtained from this study have shown that there is no significant association of ABO blood groups with diabetes mellitus but the frequency of blood group B is highest among all and lowest frequency of O and AB shown the lower risk of diabetes mellitus among these blood groups. Other results have shown the significant association of gender with diabetes mellitus the higher percentage of male in diabetic patients than females.

## REFERENCES


1. Association AD. Diagnosis and classification of diabetes mellitus. Diabetes care. 2009;32(Supplement_1):S62-S7.
2. Kadhem RC, Farawn KD, Al-Baaj MLA. Association of ABO blood groups with diabetes mellitus. Journal of Global Pharma Technology. 2018;10:192-5.
3. Ozougwu J, Obimba K, Belonwu C, Unakalamba C. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. J Physiol Pathophysiol. 2013;4(4):46-57.
4. Dave SD, Trivedi HL, Chooramani SG, Chandra T. Management of type 1 diabetes mellitus using in vitro autologous adipose tissue trans-differentiated insulin-making cells. Case Reports. 2013;2013:bcr2013200226.
5. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. The Lancet. 2018;391(10138):2449-62.
6. Kamil M, Al-Jamal HAN, Yusoff NM. Association of ABO blood groups with diabetes mellitus. Libyan Journal of Medicine. 2010;5(1).
7. Rudmann SV. Textbook of blood banking and transfusion medicine: Elsevier Health Sciences; 2005.
8. Rahman M. Non-association of ABO blood groups with diabetes mellitus in Bangladesh. Bangladesh Medical Research Council bulletin. 1976;2(2):144-6.
9. Koley S. The distribution of the ABO blood types in patients with diabetes mellitus. The Anthropologist. 2008;10(2):129-32.
10. Qureshi MA, Bhatti R. Frequency of ABO blood groups among the diabetes mellitus type 2 patients. Journal of the College of Physicians and Surgeons--Pakistan: JCPSP. 2003;13(8):453-5.

Case report

# POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME WITH BLOOD TRANSFUSION?

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**ABSTRACT**
Posterior Reverse Encephalopathy Syndrome (PRES) is a clinico-neuro-radiologic entity with various neurological manifestations, including headaches, vision problems, and altered mental status. Oedema has been observed in a generally symmetrical fashion in MRI studies, most often in the subcortical white matter and rarely in the cortex of the occipital and parietal lobes. When properly treated, this condition is usually reversible; however, failure to make a timely diagnosis may result in cerebral infarction and even death. This case report presents a 30-year-old woman with a history of postpartum bleeding and anuria, later diagnosed with PRES syndrome. This rare case is reported here for information of neurology clinicians to keep the features in mind if any such case comes up in future.

**Key Words**: Acute Kidney Injury, Posterior Reversible Encephalopathy Syndrome (PRES), Blood Transfusion

## INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES), also called reversible posterior leukoencephalopathy syndrome (RPLS), was initially described by Hinchey in 1996(1). It is characterized by several symptoms, including headache, vision change, paresis, nausea, and altered mental status(2). The pathogenesis of PRES Syndrome is still not clear. However, hypertension and endothelial injury tend to be present in almost all cases.

Here we are presenting a 30-year-old woman, gravida 3 and Para 4 came to the emergency department with complaints of anuria, loss of appetite and vomiting a day after delivering an Intrauterine death (IUD) baby at home and a history of postpartum bleeding. At the time of arrival in the emergency department, the patient was fully conscious and oriented to time, place and person. She had a pulse of 98 bpm, blood pressure of 170/100 mmHg, respiratory rate of 24breaths/minute and body temperature of 98.6°F. All systemic examinations, including the abdominal, respiratory, cardiovascular, and central nervous systems, were unremarkable. Baseline investigations including Hemoglobin were 4.3 g/dl with Mean Corpuscular Volume was 54/Fl, Total Leukocyte Count was 7.2 x 109 and Platelets count was 150 000. Sodium was 135; Potassium was 4.7mmol/L, Chloride was

103mmol/L, and Bicarbonate was 17mmol/L. Urea was 97 mg/dl, and Creatinine was 6.1 mg/dl. On ultrasound, no retained part of conception was found, and kidney size and echogenicity were within normal limits.

Our impression was Acute Kidney Injury due to postpartum haemorrhage. The treatment was started with Amlodipine 10 per day, Omeprazole 40mg, Metoclopramide, Iron Therapy, and 4 pints of Packed Cell Volumes were transfused.

On day 4th, her Urea and Creatinine were in a declining pattern, and her urine output was also improved, but the patient suddenly developed a loss of vision bilaterally. Her fundoscopic examination was normal at that time, and the other examination was unremarkable.

Her MRI brain shows T2 High Signal Noted B/L symmetrically within the Cortex and Subcortical region of both parietal and occipital lobes, which was associated with gyral swelling. These appeared low on T1W and high on FLAIR and T2W. These findings are suggestive of PRES Syndrome (Figure 1). On day 8th, she recovered her vision gradually, and 2 days later, after clinical improvement, the patient was discharged with medication and followed up in the outpatient department.

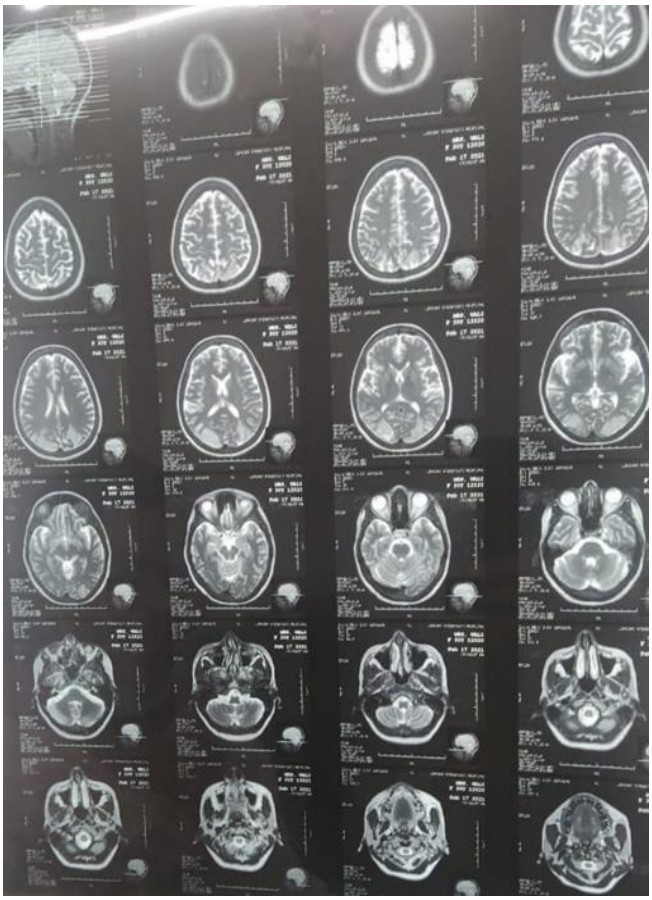

**Figure 1a. MRI Scan of the patient diagnosed with PRES Syndrome**

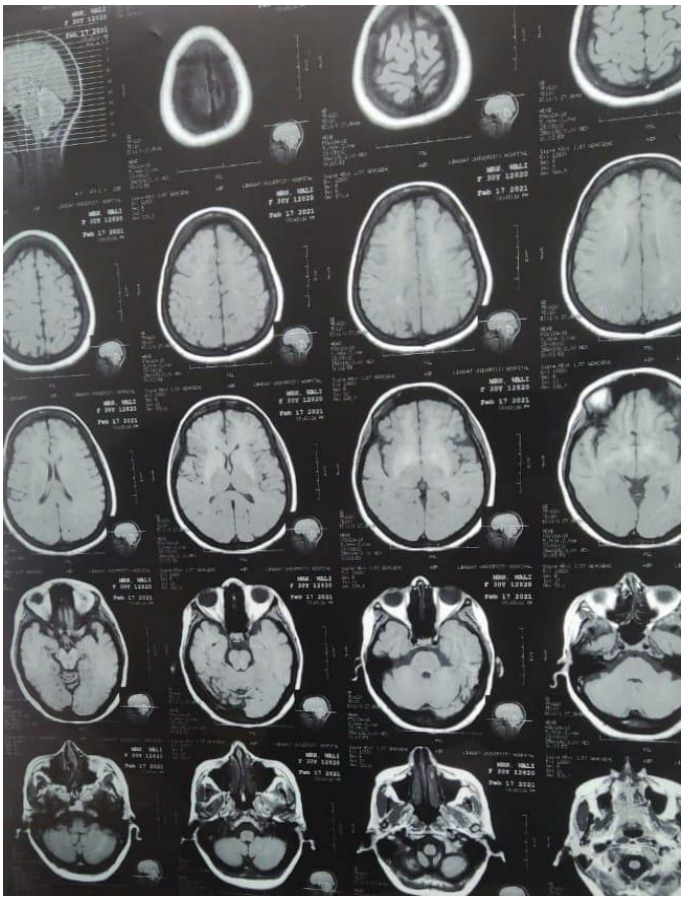

**Figure 1b. MRI Scan of the patient diagnosed with PRES Syndrome**

## DISCUSSION

Hypertension, uncomplicated and complicated pregnancies, immunosuppressive medications such as steroids, cyclosporin and tacrolimus (3), hemolytic uremic syndrome, hepatic syndrome, acute intermittent porphyria, HIV, and blood transfusion are also contributing factors for PRES syndrome. A clear female preponderance of cases exists.

The failure of autoregulation and the blood-brain barrier in the pathogenesis of brain oedema in PRES. As this posterior circulation has less sympathetic innervation than the internal carotid artery territory, it may be more vulnerable to autoregulation failure(4). The parieto-occipital area was involved in 98.7% of cases, the posterior frontal region was involved in 78.9% of cases, and according to the McKinney study, the temporal region was involved in 68.4% of patients (5).

Blood transfusions can dramatically increase overall blood volume, which can induce brain blood flow pressure. Vasogenic oedema in PRES is thought to be caused by a sudden increase in perfusion that leads to a rise in cerebral capillary perfusion pressure, ultimately exceeding the ability of the autoregulation mechanism(6).

Our patient was severely anaemic, so four pints of packed cell volume were transfused during her hospital stay. She acquired PRES syndrome a couple of days later, implying that she developed PRES syndrome due to blood transfusions. It is suspected that PRES may be a significant issue in massive blood transfusions. A high index of suspicion and timely care will help minimize morbidity and mortality and pave the way for a quick recovery. This should be borne in mind when dealing with patients needing emergency blood transfusions.

## CONCLUSION

PRES syndrome was suspected in a woman presenting with postpartum haemorrhage, and four pints of blood were transfused. Therefore, it is essential to keep in mind that such cases can be suspected after transfusion.

## REFERENCES


1. J Hinchey 1, C Chaves, B Appignani, J Breen, L Pao, A Wang, M S Pessin, C Lamy, J L Mas, L R Caplan. A reversible posterior leukoencephalopathy syndrome. N Engl J Med 1996; 334 (8):494-500.
2. C Roth , A Ferbert. The posterior reversible encephalopathy syndrome: what's certain, what's new?. Practical Neurology 2011; 11(3):136-44.
3. Susmitha Apuri , Kristin Carlin , Edward Bass , Phuong Thuy Nguyen , John N Greene . Tacrolimus associated posterior reversible encephalopathy syndrome - a case series and review. Mediterranean Journal of Hematology and Infectious Diseases 2014; 6(1)
4. Ayoub Mirza. Posterior reversible encephalopathy syndrome: a variant of hypertensive encephalopathy. Journal of Clinical Neuroscience 2006; 13(5): 590-5.
5. Alexander M. McKinney, James Short, Charles L. Truwit, Zeke J. McKinney. Posterior Reversible Encephalopathy Syndrome: Incidence of Atypical Regions of Involvement and Imaging Findings. American Journal of Roentgenology 2007; 189(4): 904-12.

6. Kei-ichiro Wada, Masayoshi Kano, Yutaka Machida, Nobutaka Hattori, Hideto Miwa. Posterior reversible encephalopathy syndrome induced after blood transfusion for severe anemia. Case Reports in Clinical Medicine 2013; 2(5):.

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