

# THROMBOCYTOPENIA DUE TO HEPARIN IN HAEMODIALYSIS PATIENTS

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## ABSTRACT

**Objective:** To study thrombocytopenia due to heparin in haemodialysis patients.

**Material and Methods:** This study was conducted in the Dialysis section of Nephrology Department Post Graduate Medical Institute, Lady Reading Hospital, Peshawar from January 2002 to December 2002. Patients with diagnosis of End Stage Renal Failure (ESRF), on maintenance haemodialysis for at least 3 months, were studied for thrombocytopenia due to heparin.

**Inclusion criteria:** Were All those patients were included in the study that were known case of End Stage Renal Failure (ESRF) and were on maintenance haemodialysis for at least three months or more. All age groups between 40 years and 60 years were included. Both male and female were included. Only Pakistani Patients were included.

**Exclusion criteria:** Were Patients on dialysis in whom the cause of renal impairment is not yet found. Patients on haemodialysis maintenance for less than three months. Thrombocytopenia in ESRF patients due to some other cause. Age group below 40 years and above 60 years were excluded.

**Results:** Total number of haemodialysis performed in 276 ESRF patients were 3675 sessions. The mean age of the patients with thrombocytopenia due to heparin was 50 years (Range 40 – 60 years). The total number of patients sustained thrombocytopenia due to heparin were 15. Nine (60%) were female and six (40%) were males. It was found that out of 276 ESRF patients who were on regular haemodialysis only nine (3.2%) patients had complications due to thrombocytopenia because of heparin.

**Conclusion:** Thrombocytopenia due to heparin was studied for the first time in NWFP and it was found that a minority of patients on maintenance haemodialysis develop thrombocytopenia due to heparin.

**Keywords:** Haemodialysis, End Stage Renal Failure, Thrombocytopenia, Heparin.

## INTRODUCTION

There is a continuing expansion in the number of patients with ESRF. The majority are unsuitable for transplantation because of underlying co-morbid conditions, unavailability of transplant donor, delayed referral of a patient with ESRF to nephrologists or lack of resources for renal transplantation and subsequently post transplant immunosuppressive therapy. This all results in increasing number of patients receiving long – term haemodialysis.

Thrombocytopenia due to heparin is a relatively common side effect of heparin and can cause substantial morbidity & mortality in haemodialysis patients<sup>1</sup>.

There are two clinical entities of thrombocytopenia.

- a). **Type I :** is a harmless pharmacological phenomenon, seen when platelets fall in the first 24 – 48 hours after starting heparin. It never leads to thrombosis and does not necessitate stopping heparin<sup>2</sup>.
- b). **Type II:** is the most important and frequent drug induced thrombocytopenia. It is mediated by antibodies against the heparin-platelet-factor-4 (PF4) complex.

Thrombocytopenia itself rarely cause complications but the disorders associated with it are potentially life threatening. Venous thrombo-embolism occurs in about

### Demography of the study

Age group	Female n = 9	Male n = 6
40 - 45 years	3 (33.3%)	1 (16.6%)
46 - 50 years	2 (22.2%)	1 (16.6%)
51 - 55 years	2 (22.2%)	2 (33.3%)
56 - 60 years	2 (22.2%)	2 (33.3%)

Table 1

50% of patients with type II. Other significant complication include skin reactions at the site of injection, disseminated intravascular coagulation (DIC), cerebral thrombosis, myocardial infarction and ischemic limbs<sup>3,4</sup>.

Diagnosis of thrombocytopenia due to heparin (Type II) depends on exclusion of other conditions associated with thrombocytopenia and on the demonstration of heparin - induced antibodies (HIA) in the plasma<sup>5</sup>.

This study was carried out to study the thrombocytopenia due to heparin in haemodialysis patients.

### MATERIAL AND METHODS

We studied 276 patients of End Stage Renal Failure (ESRF) on maintenance haemodialysis for 3 months or more, from January 2002 to December 2002. This study was performed in the dialysis section of Nephrology Department, Post Graduate Medical Institute, Lady Reading Hospital, Peshawar.

Clinical details of patients with ESRF were studied as age, sex, duration of dialysis to diagnosis, signs of thrombocytopenia & platelet count along with serum chemistry in each patient before scheduled haemodialysis session.

### RESULTS

During the study period for January 2002 to December 2002, we studied 276 patients with ESRF, who were on maintenance haemodialysis since 3 or more months and anticoagulant used

during haemodialysis sessions was heparin. We had 15 (5.4%) cases of thrombocytopenia due to heparin (9 female & 6 males, 40 – 60 years of age, means 50 years). See table 1.

Nine (60%) patients with thrombocytopenia due to heparin had complications of the syndrome, with each one of the following. Petechial rash, retroperitoneal haematoma, deep vein thrombosis and two patients had sudden death & on clinical grounds were diagnosed as pulmonary embolism. Six (40%) patients had no complication. See table II.

### DISCUSSION

Study on thrombocytopenia due to heparin in haemodialysis patients is conducted for the first time in Pakistan. We assessed 276 ESRF patients for the syndrome & could find in only 15 patients. In general population it has been demonstrated that type – II thrombocytopenia is less common in medical patients than surgical patients (0.7% Vs 5%) and has a lower incidence with low molecular weight heparins than un-fractionated heparin (UH) (0.5% Vs 5%)<sup>6</sup>.

Our finding of 15 cases out of total of 276 patients suggests that dialysis patients have a lower risk of thrombocytopenia (Type-II) than the general population due to the fact that there is impaired immunity of dialysis patients or the haemodialysis patients are exposed to smaller dose of heparin in the extra corporeal circuit compared with the therapeutic heparin in general patients. This is also supported by Chang & Parikh<sup>7</sup>. Previously it has been shown that bovine heparin has a higher incidence of type – II thrombocytopenia than porcine but now all over the world porcine heparin is used in dialysis population. There may be other variable factors responsible for the syndrome such as quantity of the heparin and type given (unfractionated heparin or low molecule weight heparin)<sup>8</sup>.

Several groups have demonstrated that thrombocytopenia due to heparin in haemodialysis patients is associated with increased morbidity & mortality<sup>9</sup> but in our study it was found that only minority of haemodialysis patients diagnosed with

### Complications of the thrombocytopenia due to heparin

Complication	No. of patients n = 9	%age
Petechial rash	3	33.3%
Retroperitoneal haematoma	1	11%
Deep vein thrombosis (DVT)	3	33.3%
Pulmonary embolism (P.E)	2	22.2%

Table 2

thrombocytopenia due to heparin had reported complication (9 patients) (3.2%).

## CONCLUSION

1. We have found that ESRF patients have delayed onset & only minority of patients (ESRF) developed complication.
2. As described in other studies dialysis patients have a lower risk of thrombocytopenia (Type-II) than the general population due to the fact cited above.
3. More studies are required to establish the results and to correlate them internationally.

## REFERENCES

1. Aster RH. Heparin-Induced Thrombocytopenia and Thrombosis. *N Engl J Med* 1995; 332: 1374
2. Haase M, Bellomo R, Rocktaeschel T et al. Use of fondaparinux (ARIXTRA (R)) in a dialysis patient with symptomatic heparin induced thrombocytopenia type II. *Nephrol Dial transplant* 2005; 20: 444.
3. Aster RH. Drug-induced immune thrombocytopenia: an overview of pathogenesis. *Semin Hematol* 2005; 36.
4. Mattioli A. Prevalence of anti-PF4/heparin antibodies and the HIT syndrome in cardiovascular medicine. *Semin Thromb Hemost* 2004; 30: 291.
5. Keeling D, Davidson S, Watson H. Haemostasis and Thrombosis Task Force of the British Committee for Standards in Haematology. The management of heparin induced thrombocytopenia. *Br J Haematol* 2006; 133: 259.
6. Warkentin TE, Levin MN, Hirsh J. Heparin-Induced thrombocytopenia in Patients Treated with Low-Molecular weight Heparin or Unfractionated Heparin. *N Engl J med* 1995; 332: 1330.
7. Martel N, Lee J, Wells PS. Risk for heparin-induced thrombocytopenia with unfractionated and low-molecular weight heparin thromboprophylaxis: a meta-analysis. *Blood* 2005; 106: 2710.
8. Samuelsson O, Amiral J, Attman PO. Heparin-induced thrombocytopenia during continuous haemofiltration. *Nephrol Dial Transplant* 2005; 10: 1768.
9. Mureebe L, Coats RD, Silliman WR, Shuster TA, Nichols WK, Silver D. Heparin-associated antiplatelet antibodies increase morbidity and mortality in haemodialysis patients. *Surgery* 2004; 136: 848.

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