

# PLATELET ANTIBODIES IN VARIOUS DISEASES

Thesis

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By

OMAYMA ABD EL-MAGUID LOTFY  
(M.B., B.Ch and M.Sc.)

Supervised by

610 07561

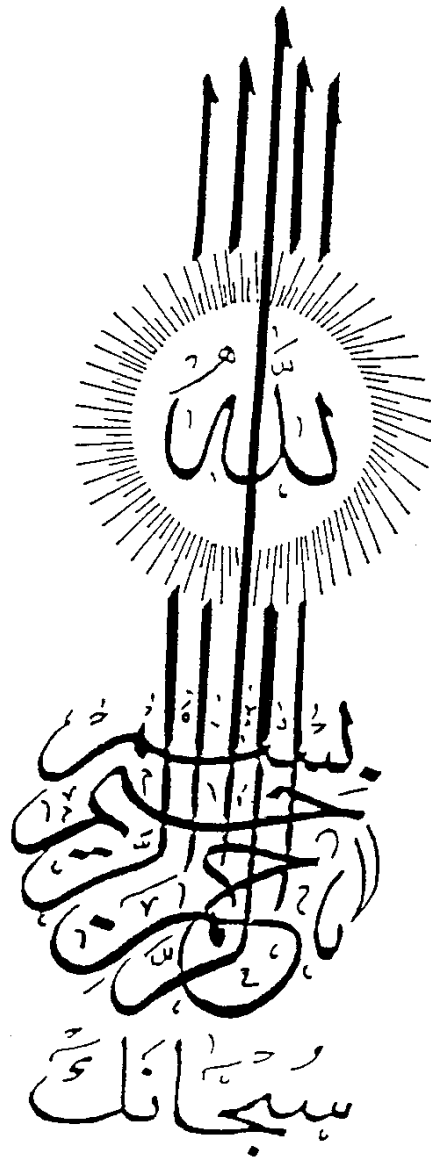
PROF. DR. AIDA ABD EL-AZIM  
Professor of Clinical Pathology

PROF. DR. LAILA EL-SHAWARBY  
Professor of Clinical Pathology

PROF. DR. SALWA YOUSSEF  
Professor of Clinical Pathology

DR. SALWA ABU EL-HANA  
Assistant Professor of Clinical Pathology

FACULTY OF MEDICINE  
AIN SHAMS UNIVERSITY  
1992



لَا عِلْمَ لَنَا إِلَّا بِمَا عَلَّمْنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ  
صَدَقَ اللَّهُ الْعَظِيمُ

سورة البقرة آية ٢٠



*TO MY FAMILY*

امانی / احمد  
صبا

نجوى محمد عبد المنعم

ماجد / محمد

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## LIST OF ABBREVIATIONS

- AIDS : Acquired immunodeficiency syndrome.
- AITP : Autoimmune thrombocytopenic purpura.
- C : Complement.
- CELIA : Competitive enzyme linked immunosorbent assay.
- CLL : Chronic lymphocytic leukemia.
- DIIT : Drug-induced thrombocytopenia.
- DTS : Dense tubular system.
- ELISA : Enzyme linked immunosorbent assay.
- Fab : Fraction antigen binding.
- Fc : Fraction crystallizable of the immunoglobulin.
- GM-CSF : Granulocyte-macrophage colony stimulating factor.
- GP : Glycoprotein.
- HLA : Human leucocyte antigen.
- IL : Interleukin.
- ITP : Idiopathic thrombocytopenic purpura.
- MAIPA : Monoclonal antibody immobilization platelet antigens.
- Meg-CSF: Megakaryocyte colony stimulating factor.
- MPV : Mean platelet volume.
- MSF : Megakaryocyte stimulating factor.
- NAIT : Neonatal autoimmune thrombocytopenia.
- P Abs : Platelet antibodies.
- PAIg : Platelet associated immunoglobulin.
- PTP : Post transfusion purpura.
- SCCS : Surface connected canalicular system.
- TSF : Thrombopoietin stimulating factor.

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# INTRODUCTION AND AIM OF THE WORK

## INTRODUCTION AND AIM OF THE WORK

Recent studies by several groups of investigators have shown that platelet antibodies, either bound to the surface of platelets or free in the serum, were sought in patients who had low platelet counts for a variety of reasons.

The hypothesis has been put forward that elevated surface platelet associated immunoglobulins represent autoantibodies bound to the circulating platelets *in vivo* and has a role in the increased platelet destruction by immune mechanism (McMillan, 1990).

Moreover, the platelet damaging effect of thrombocytophlyic circulating immune complexes has been postulated (Kiefel et al., 1986).

The role of complement in the pathogenesis of the immune mediated platelet destruction remains uncertain (Bussel, 1990). However, elevated platelet antibodies (PAIgG) has not only been found in thrombocytopenia suspected to be due to an immunological process, but also in patients with thrombocytopenia of presumably non immunological etiology (George, 1990).

Furthermore, raised levels of platelet antibodies was noticed in thrombocytopenia as well as in non thrombocytopenia of various disorders (Puram et al., 1984). However, there may be causes other than specific immune binding that could contribute to the increased levels of surface platelet immunoglobulins as altered membrane properties, increased mean platelet volume (MPV) (Holme et al., 1988). The raised level of surface platelet immunoglobulins may be a reflection of elevation of serum IgG (George and Saucerman, 1988).

Thus, the present study aimed to measure the amount of serum platelet antibodies (serum platelet IgG) by mean of an ELISA technique and to evaluate its significance in thrombocytopenic as well as in non thrombocytopenic patients with various disorders. Correlation of the level of platelet antibodies to platelet count, MPV as well as to serum IgG, immune complexes (ICs), C3 and C4 will be studied.

# REVIEW OF LITERATURE

## PLATELETS

### PLATELET MORPHOLOGY:

The blood platelets in man circulate as flattened anucleated disc-shaped cells at a concentration of  $250 \times 10^9/L$  (range 150 to  $400 \times 10^9/L$ ). Normal platelets measure  $3.6 \pm 0.7 \mu m$  in diameter,  $0.9 \pm 0.2 \mu m$  in thickness with a platelet volume ranging from 7 to 9 fl (Frojmovic and Milton, 1982).

The platelets in the peripheral blood are heterogeneous in respect to size, density and staining characteristics. In polychrome-stained smears, the blood platelet is round, oval or rod shaped. The cytoplasm is a clear blue (hyalomere) and contains a few fine azurophilic granules (granulomere).

Variations in platelet size and morphology can be seen in a variety of disorders, e.g., in autoimmune thrombocytopenia, myelofibrosis and certain forms of thrombocytopenia associated with disordered platelet function (Bithe11, 1987).

### Mean Platelet Volume (MPV): Evaluation and Clinical Utility:

The mean platelet volume represents the average of the volume of platelet. In seeking to establish reference values for normal subjects with normal platelet counts, MPV was found to be  $7.8 \pm 1.8$  fl (Rowan, 1983).

The initial regulation of platelet volume in response to acute reduction of the platelet mass occurs through process that governs platelet release rather than growth of megakaryocyte cytoplasm or alterations in megakaryocyte ploidy (Corash et al., 1990).

Several studies of platelet size in response to cessation of platelet production have suggested that platelets decrease in size as they age in the circulation (Ginsburg and Aster, 1972). Recent data, however, have demonstrated that platelets do not change in volume significantly as they age in the circulation during steady-state thrombopoiesis (Harris and Penington, 1984).

MPV is an easily obtained variable that appears to be useful in the evaluation of abnormal platelet production. In 1974, O'Brien noted that the platelet count and MPV were inversely related. This observation has been confirmed by others (Levin and Bessman, 1983).

MPV has been used to distinguish between thrombocytopenia resulting from peripheral destruction where there is an increase in the MPV from that due to bone marrow damage (cytotoxic chemotherapy) where the MPV is decreased (Nelson and Kehl, 1981).

Previous studies that have demonstrated a decrease in the MPV of circulating platelets following radiation or chemotherapy may reflect an alteration in normal platelet physiology as a result of these therapies, or a selective consumption of larger platelets as a result of increased haemostatic demands (Thompson and Jakubowski, 1988).

In autoimmune thrombocytopenia, the increased thrombopoietic stimulation is accompanied by a parallel increase in platelet volume and in individual patients the course of thrombocytopenia is accompanied by inverse changes of platelet volume (George, 1990). In severe platelet destruction large stress platelets or proplatelets appear in the circulation (Thompson and Jakubowski, 1988). Platelet fragmentation causing microplatelets has also been defined in some cases of autoimmune thrombocytopenia (Zucker-Franklin and Karparkin, 1977).

#### Aspects of Platelet Ultrastructure (Fig. 1):

##### *The Plasma Membrane:*

Morphologically, it consists of the unit membrane and an exterior coat, the glycocalyx. The bilayer unit membrane is composed of phospholipid and proteins (Hovig, 1989).

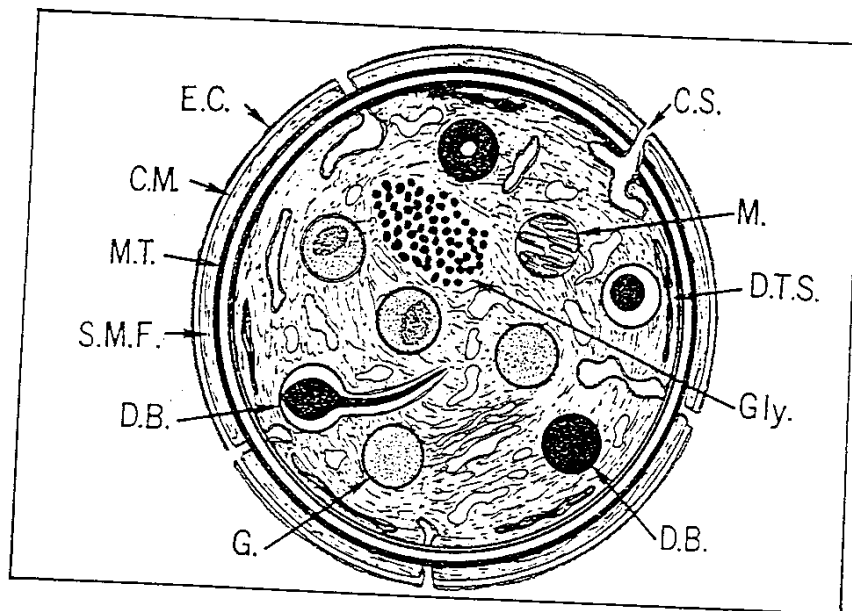


Figure (1): Platelet ultrastructure.

- EC : Exterior coat.
  - CM : Cell membrane.
  - MT : Microtubule area.
  - SMF: Submembrane filament area.
  - DB : Dense bodies.
  - G : Platelet granules.
  - CS : Canalicular system.
  - M : Mitochondria.
  - DTS: Dense tubular system.
  - Gly: Glycogen.
- (Quoted from Hovig, 1989).