Deep vein thrombosis and its sequel pulmonary embolism collectively termed venous thromboembolism are associated with significant morbidity and mortality. Clinical diagnosis is inherently insensitive and inaccurate because of common signs and symptoms of the disease overlap considerably with other conditions. It is unacceptable to diagnose DVT&PE clinically and commit patients to the risk of anticoagulants without objective confirmatory testing.

Various diagnostic algorithms that emphasize noninvasive and cost effective strategies have been evaluated. The discovery of single laboratory marker that would either confirm diagnosis or rule out the disease can be considered the holy grail of clinical medicine.

Deep vein thrombosis of lower extremity usually begins in the deep veins of the calf around the valve cusps or within soleal plexus. A minority of lower extremity DVT arise in the iliofemoral system as a result of direct injury to the vessel wall as seen in hip surgery and catheter induced DVT. The vast majority of calf vein thrombosis dissolve completely without therapy. Approximately 20% propagate proximally. The propagation usually occurs before embolization.

The process of adherence and organization of venous thrombosis does not begin until 5-10 days after thrombus formation, until this process has been fully established the non-adherent disorganized. Thrombus may propagate and or embolize. Asymptomatic DVT is found in 40-50% of patients with PE. 40% of patients with DVT have clinically silent PE based on objective studies.

Venous thrombosis is a chronic disease, and recurrent events are fatal in approximately 5% to 9% of patients. Predicting the likelihood of recurrence in an individual patient is of utmost importance, because most recurrences can be prevented by antithrombotic therapy. The presence or absence of certain clinical and laboratory patient characteristics determines a low or high recurrence risk. The risk is low among patients with venous thromboembolism (VTE) provoked by surgery, trauma, immobilization, pregnancy, or female hormone intake, whereas it is higher among those with unprovoked thrombosis. Stratification of patients with unprovoked VTE according to their recurrence risk can be achieved on the basis of clinical risk factors including patient's sex, comorbidities, or overweight or by measuring laboratory markers of thrombophilia such as factor V Leiden, the prothrombin mutation, natural coagulation inhibitor deficiencies, elevated coagulation factors, and antiphospholipid antibodies. A novel approach to assess the recurrence risk is the use of global coagulation markers, including D-dimer, or in vitro thrombin generation.

Venous thrombosis activate both the coagulation system and fibrinolytic system result in elevated level of serum markers collectively called fibrin split products. During thrombus formation fibrinogen convert to fibrin monomers that are extensively cross linked into polymer network, this cross linking of fibrin takes place in the region of polymer termed D-domain. Adjacent D-domains are covalently linked and constitute fibrin, specific feature of thrombus not found in fibrinogen or non-cross linked form fibrin degradation products.

Fibrin polymers are degraded by plasmin in the fibrinolytic system forming D-dimer. Monoclonal antibody to D-dimer have been developed that can differentiate fibrin specific clot from non crosslinked fibrin as well as fibrinogen, on other hand these antibodies are specific for both freshly formed fibrin clots as well as fibrinolysis product, this specific characteristic of D-dimer explain its high sensitivity for venous thromboembolism. D-dimer level are elevated in acute phase of clot formation in acute DVT as well as during fibrinolytic stage which occur in PE. D-dimer with half-life 4-6 hours and remain elevated for the next 7 days. Once clot organization and adherence begin the D-dimer start to be reduced. Patients with isolated calf vein clots have no D-dimer levels.
thrombosis which may has small clot burden that result in low level of D-dimer fall below the level of detection. This explains false negative D-dimer assay in setting of confirmed calf vein thrombosis. New D-dimer assays are quantitative and quick. The Instant IA D-dimer from Diagnostica Stago and Nycocard D-dimer from Nycomed Pharm take only about 10 minutes to produce results.

The Vidas D-dimer from bioMérieux takes 35 minutes. The whole blood agglutination SimpliRED assay from Agen Biomedical is the fastest—yielding results in only two minutes. It is done with a drop of whole blood, so it doesn’t require centrifuging blood to separate out plasma.

All these D-dimer assays have a high sensitivity for deep venous thrombosis and pulmonary embolism. The rapid ELISA assays Nycocard and Instant IA achieved a sensitivity of 94.3 percent in two studies with a total of 213 patients with clinically suspected DVT and a sensitivity of 96 percent in three studies of 592 patients with suspected PE. SimpliRED had a sensitivity of 89 percent in one study of 214 patients with signs of DVT; and, in two studies including 1,263 patients, SimpliRED had a sensitivity of 89 percent for pulmonary embolism (Thromb Haemost. 1999; 888-692). Those tests provided by coromy 200 accent can reach sensitivity up to 95% within 30 minutes.

The plasma levels of D-dimer were found to be directly related to the severity of PE and could predict adverse outcomes assessed by radiologic, biochemical, and clinical criteria. Furthermore, markedly elevated D-dimer levels were recently found to increase the likelihood of PE diagnosis. Thus, high D-dimer levels upon presentation may potentially prompt a more intense diagnostic approach, irrespective of pretest probability.

Elevated plasma levels of D-dimer antigen gradually normalize in patients receiving anticoagulant therapy for acute VTE. In an attempt to study these changes, patients were randomized to receive either dose-adjusted unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH). In this instance, no significant difference in the rate of normalization of markers of coagulation activation (including D-dimer) was noted. This observation suggests that the use of agents with predominantly anti-Xa activity (LMWH) or agents with combined anti-Xa and antithrombin activity (UFH), results in equivalent changes in fibrin formation and degradation after acute thrombosis. In theory, plasma “D-dimer antigen” levels could thus be used to monitor the response to therapy using either agent. However, on the basis of the current evidence, there is generally no compelling reason to track D-dimer antigen levels during the initial phase of anticoagulation.

Methods, this study, carried out in the geoden lab in the period between July 2011 and end in July 2013. All patients had DVT. A total of 30 patients had been investigated for D-dimer level. 17 patients out of 30 had positive Doppler imaging while the remaining 13 patients showed negative Doppler results. All patients had been investigated within 7 days from the beginning of the complaints to avoid the false negative results. The D-dimer measured by mean autoanalyzer machine coromy accent 200. D-dimer level of less than 0.5 iu/ml as the cutoff point. The principle of the test done on patients serum. 17 normal and healthy person had been chosen as control group. The statistical analysis was done by using SAS system 2010.

Results.

Table 1: Patients Characteristics.

<table>
<thead>
<tr>
<th>Patients number</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (22-70) years</td>
<td>Mean 42.3 years</td>
</tr>
<tr>
<td>Sex</td>
<td>Male (9) 30% Female (21) 70%</td>
</tr>
</tbody>
</table>

Table 2: D-dimer level.

<table>
<thead>
<tr>
<th>Patients group</th>
<th>Range (0.18-6)iu/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Mean (2.56 ± 0.29)</td>
</tr>
<tr>
<td>Mean (0.294 ±0.02)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: The relationship between D-dimer level and Doppler imaging.

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Doppler</th>
<th>D-dimer level</th>
<th>D- dimer mean level</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>Positive</td>
<td>Positive</td>
<td>3 ± 034</td>
</tr>
<tr>
<td>11</td>
<td>Negative</td>
<td>Positive</td>
<td>2.26 ± 0.03</td>
</tr>
</tbody>
</table>

Table 4: Patients show no objective results.

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Doppler</th>
<th>D-dimer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>
Discussion. In this series of thirty patients with deep vein thrombosis all are tested for D-dimer concentration within 7 days from onset of symptoms. The incidence of DVT in the general population has been reported to be about 1/1000/ year. The pathogenesis of DVT is quite complex, hyperactive coagulation pathway or hypoactive anticoagulant mechanism and or hypoactive fibrinolysis being all implicated.

DVT appears to be multicausal disease that’s more than single risk factors need to be present simultaneously to cause thrombosis. The risk factor incriminated includes acquired and genetic factors.

Known acquired risk factors include immobilization, surgery, trauma, pregnancy, puerperium, lupus anticoagulant, malignancy and female hormone10.

Among the genetic factors carry a tendency to VT are anti thrombin11 deficiency, protein c deficiency, protein s deficiency, factor v leiden, prothrombin 20210A mutation and homocystenemia.

New methods based on immunological markers carry sensitivity up to 95%. On the other hand negative D-dimer in patients with low risk for thrombosis can rule out diagnosis of deep thrombosis.

Table 2 shows the wide difference in level in level of D-dimer in DVT compared to control group, this increase the sensitivity of D-dimer in the diagnosis of DVT11.

Table 3 shows 11 patient out of 30 (36.6%) shows positive D-dimer in patients with negative Doppler imaging with mean level 2.26iu/ml (cut off less than 0.5). On other hand those patients with positive Doppler 17 patients out of 30 (56.6%) with mean of D- dimer 3iu/ml this may suggest that higher level of D-dimer may denote large clot that can be seen easily by Doppler.

The remaining two patients ,table 4, out of 30 (6.6%) show a pitfall mostly due to small thrombi or those in the venous junctions that cannot be seen by Doppler with late presentation after D-dimer normalization, both patients are presented post-delivery which increase the possibility of delay in time of intervention.

From the result of this study, we conclude that, patients with suspicious feature of deep thrombosis and negative, Doppler results should be investigated serially for D-dimer using more sensitive principle based on immunological assay which had sensitivity up to 95% and avoid those methods which depend on latex test or whole blood that carry sensitivity no more than 45%. On the other hand time delay should be avoided as much as possible. The negative result of D-dimer in absence sign and symptoms of thrombosis can roll out diagnosis of DVT.

References

1. Donald H. schreiber. Laboratory medicine february 2000 number2 volume32 136-140.