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## BRIEF REPORTS

# Utility of D-dimer level as an analytical marker in pediatric emergencies

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### CONFLICT OF INTEREST:

None

**Objectives:** To describe our experience using D-dimer levels in attending pediatric emergencies.

**Methods:** For this retrospective descriptive study we reviewed all emergency patient records in which D-dimer levels were measured in 2005 and 2006. We compiled descriptive statistics and analyzed the association between levels of D-dimer and C-reactive protein (as a marker of inflammatory response) using a nonparametric correlation test.

**Results:** Rash and fever were the main reasons for attending the emergency room. The D-dimer level was elevated in 34.3% of the cases. D-dimer and C-reactive protein levels were not correlated. The D-dimer level was elevated in 71% of the patients with sepsis.

**Conclusions:** D-dimer elevation is a nonspecific marker in certain inflammatory processes. It is difficult to interpret, may lead to confusion, and should be read in a manner that is consistent with the clinical context. Prospective studies are needed to provide evidence of its utility as a marker in acute conditions in children. [Emergencias 2009;21:28-31]

**Key words:** D-dimer. Emergency Service, Hospital. Fibrinolysis. Sepsis.

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## Introduction

D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. Elevated DD values are detected in plasma at onset of thrombus formation and remain high during approximately one week<sup>1</sup>. This explains why it is possible to find elevated DD in situations of increased fibrinolytic activity. It is present in many clinical conditions, especially deep venous thrombosis and pulmonary embolism, but also in myocardial infarction, disseminated intravascular coagulation, pneumonia, cardiac failure, neoplasia, polytrauma or in patients after surgery<sup>2</sup>.

Studies on the statistical power of DD as an analytic marker of deep venous thrombosis and pulmonary thromboembolism conclude that DD test has high sensitivity and low specificity (98-100% and 35-39%, respectively)<sup>3</sup> and high negative predictive value<sup>4</sup>. Thus, DD is useful for ruling out deep venous thrombosis and pulmonary thromboembolism, but not for confirmation of their presence. All these studies were performed

in adults. In children, deep venous thrombosis and pulmonary thromboembolism are rare. Although infrequent in children, arterial or symptomatic venous thromboses are more frequent in neonates, probably because they present lower levels of physiological inhibitors of coagulation and less fibrinolytic capacity than older children<sup>1</sup>. Various studies indicate the high negative predictive value of DD for recurrence after a thrombotic event<sup>5,6</sup>.

Apart from thrombotic disease control, more appropriate for adults, the known utility of DD in children is for follow up of severe conditions, one of which is haemolytic uremic syndrome<sup>7,8</sup>. The main mechanism of diarrhoea associated to haemolytic uremic syndrome is thrombotic microangiopathy. In these children there is limited intravascular coagulation with elevated DD<sup>9,10</sup>. DD is also elevated in disseminated intravascular coagulation and has been described in cases of cranial trauma<sup>11</sup>. Similarly, the utility of DD has been described in children with nephritic syndrome as an indicator of predisposition to thromboembolism<sup>12-14</sup>.

All the above-mentioned indications corres-

pond to evolution control in diverse diseases; however, there are no clear data on the utility of DD as a diagnostic and prognostic tool in acute processes. Given the empiric use of DD in our paediatric emergency department, we wished to investigate its real utility in paediatric patients attended by our ED. We report the most frequent medical conditions diseases where DD is habitually determined and the cases where it is found to be elevated.

Also, we wished to determine the relation between high DD values and C reactive protein (CRP), since CRP is an acute phase reactant often used in our ED to help determine systemic inflammatory activity.

## Method

For this retrospective descriptive study we reviewed all emergency patient records in which D-dimer levels were measured in 2005 and 2006. The following variables were recorded: reason for visit, DD value, platelet count and prothrombin activity, definitive diagnosis and need for admission.

DD was determined in our centre using turbidimetric test in citrated plasma. The test was considered positive when values were  $> 500 \mu\text{g/l}$ . CRP was determined by coagulation assay. The data obtained were stored on a data base, respecting patient data confidentiality in accordance with the law ("Ley Orgánica 15/1999, and R.D. 994/99").

We present a statistical description of the continuous variables. To determine the correlation between DD and CRP, the variables proved to have an abnormal distribution normal and were therefore analysed using the corresponding non-parametric test (Spearman's rho). Statistical analysis was performed with SPSS 9.0 (SPSS Inc.).

## Results

DD was determined in 168 patients, for whom we were able to access 137 clinical histories. The most frequent reason for consulting ED was exanthema (82 cases) followed by self-limited febrile syndrome (37 cases). The remaining reasons are shown in Table 1. The most frequent diagnoses were: non-specific exanthema (40 cases) and self-limited febrile syndrome (19 cases); the remaining diagnoses are shown in Tables 1 and 2. Clinical pictures considered to be of probable virosis were: slight infection (mainly, self-limited febrile syndrome without evident focus, sudden exanthema and upper respiratory pathway catarrh) without demonstrated bacterial aetiology.

DD was elevated ( $> 1000 \mu\text{g/l}$ ) in 47 cases (34.3%) with a mean value of  $1410.8 \mu\text{g/l}$  (Table 2). The highest values corresponded to cases of sepsis ( $6,936 \mu\text{g/l}$ ), acute pyelonephritis ( $6,005 \mu\text{g/l}$ ), viper bite ( $5,068 \mu\text{g/l}$ ), acute urticaria ( $2,977 \mu\text{g/l}$ ), myositis ( $1,880 \mu\text{g/l}$ ), arthritis ( $1,939 \mu\text{g/l}$ ), pneumonia ( $2,940 \mu\text{g/l}$ ) and appendicitis ( $1,658 \mu\text{g/l}$ ).

Regarding the relation between DD and the acute phase reactant CRP, 30% of the cases with positive DD had elevated CRP ( $> 25 \text{ mg/L}$ ), and 30% of those with elevated CRP had negative DD corresponding to cases of sepsis, cellulitis and viriasis, among others. The cases with the highest CRP values (sepsis, pneumonia, meningitis) did not show elevated DD (Figure 1). The correlation between DD and CRP (Spearman Rho test) revealed a positive tendency; as the value of CRP increased, so did that of DD. However, the correlation coefficient was 0.362 which indicated that there was no significant association between these two variables.

**Table 1.** Reasons for consulting and final diagnoses in patients where D-dimer levels were determined

Reason for visit	N	Diagnosis
Exanthema	82	Non-specific (40), urticaria (3), idiopathic thrombocytopenic purpura (4), tonsillitis (5), pneumonia (1), leukaemia (1), other (28).
Fever	37	Self-limited febrile syndrome (19), pneumonia (7), AGE (1), viral meningitis (2), PNA (5), myositis (3).
Abdominal pain	6	AGE (4), pneumonia (1), appendicitis (1).
Viper bite	2	Self-limited bite (2).
LL pain, suspected DVT	3	Arthritis (2), non-specific pain (1).
Other	7	Probable viriasis (6), pneumonia (1).

N: number of cases with each diagnosis. ITPI: idiopathic thrombocytopenic purpura. AGE: acute gastroenteritis. LL: lower limbs. DVT: deep venous thrombosis.

**Table 2.** Final diagnoses and positive D-dimer (DD)

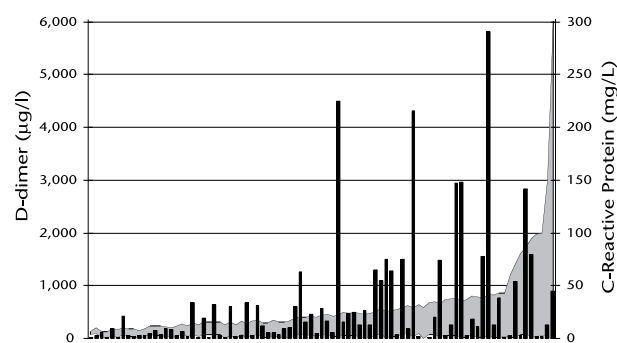
Diagnosis	N	DD > 500 µg/l (% positive)
Arthritis	2	1 (50)
Pneumonia	9	5 (56)
Probable viriasis	73	26 (35.6)
Myositis	3	1 (33.3)
Acute Pyelonephritis	5	4 (80)
Viral Meningitis	2	1 (50)
Appendicitis	1	1 (100)
Bite	2	1 (50)
Urticaria	3	2 (67)
Sepsis	7	5 (71.4)

## Discussion

This study presented certain limitations typical of retrospective studies, including the difficulty of obtaining complete data. In addition, it was a single-centre study and DD determination in our hospital is not standardised. However, it proved useful for the analysis of DD as a marker of inflammation and allows certain conclusions to be drawn.

Elevated DD is frequently found in inflammatory processes, but always in a non-specific way (appendicitis, pneumonia, arthritis, myositis, meningitis and pyelonephritis) and is not significantly associated with acute phase reactants such as CRP. It is also elevated in apparently viral processes, mostly accompanied by non-specific petechial exanthema. This may be due to isolated alterations of coagulation in those cases. Elevated DD in sepsis has been previously reported, associated with disseminated intravascular coagulation disorder<sup>11</sup>. A striking finding was elevated DD in bites and urticarial reactions, probably due to local and self-limited changes in coagulation.

The interpretation of elevated DD is often difficult and may lead to confusion, of little use for diagnosis. It must be interpreted within the clinical context and taking into consideration other factors such as CRP, thrombocytosis or thrombopenia and decreased prothrombin activity, among others. Further studies are required to demonstrate the utility of DD as an analytic marker of inflammation in acute paediatric processes and to validate this parameter as a diagnostic tool in paediatric emergency services.

**Figure 1.** Correlation between D-dimer (curve) and C reactive protein (bars).

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## Utilidad del dímero D como marcador analítico en urgencias pediátricas

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**Objetivos:** Describir nuestra experiencia acerca del uso del dímero D (DD) en urgencias pediátricas.

**Método:** Se realiza un estudio descriptivo, retrospectivo. Revisamos todas las historias clínicas de urgencias de nuestro centro en las que se realizó determinación analítica del DD durante los años 2005 y 2006. Describimos los datos obtenidos y analizamos estadísticamente la asociación del DD con un parámetro de respuesta inflamatoria (la proteína C reactiva) mediante un estudio de correlación no paramétrico.

**Resultados:** Los principales motivos de consulta, en las 137 historias revisadas, fueron exantema y fiebre. El DD resultó positivo en el 34,3% de los casos. No se halló correlación estadísticamente significativa entre el DD y la proteína C reactiva. El DD fue positivo en el 71% de los casos de sepsis.

**Conclusiones:** El DD se eleva en algunos procesos inflamatorios, de manera inespecífica. Su interpretación es difícil y puede llevar a confusión. Es necesario analizarlo en su contexto clínico. [Emergencias 2009;21:28-31]

**Palabras clave:** Dímero D. Urgencias. Fibrinólisis. Sepsis.