

Invasive Meningococcal Disease in two Italian regions: a prediction of the risk of death

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Background. The Invasive Meningococcal Diseases (IMD) incidence in Europe is decreasing, showing an average incidence of 0.68/100.000 population mainly due to Serogroup B followed by Serogroup C. However, during 2015-2016 biennium, Tuscan Region has been affected by an IMD epidemic outbreak caused by Serogroup C *Neisseria meningitidis* hypervirulent Sequence Type 11 clonal complex (ST-11 cc).

Methods. 67 patients (male 63% - median age 31±21 years) with an IMD developed in Tuscany Region and in Cotugno Hospital of Naples, from January 2015 to August 2016, were enrolled in this study. We analyzed the underlying patient's characteristics, risk factors and clinical characteristics. To predict the risk of death we fit a multivariate logistic regression with a gradient boosting approach. As a result, the odds ratios (OR) of the selected variables were computed.

Results. Demographics, main clinical characteristics, antibiotic therapy during IMD and outcome of study population are summarized in Table 1. In Tuscany cluster older patients, more Serogroup C and purpura fulminans were more frequent. Furthermore IgM enriched Immunoglobulin treatment markedly reduced (about 57%, OR 0.429) the probability of death, while septic shock (OR 2.261) appeared as the strongest risk factor for death, and a role has been found for SOFA score (OR 1.269), Serogroup C (OR 1.241), age (OR 1.010) and purpura fulminans (OR 1.062).

| | Patients (n = 67) | Overall Survival (n = 59) | Overall Death (n = 8) | p |
|--|----------------------|------------------------------|--------------------------|--------|
| Tuscany region | 32/67 (48%) | 25/59 (42%) | 7/8 (88%) | 0.043 |
| SOFA | 4 [2-7] | 4 [2-6] | 10 [10-11.5] | <0.001 |
| Serogroup C | 31/67 (46%) | 24/59 (41%) | 7/8 (88%) | 0.034 |
| Δ Time from onset of symptoms to begin empirical antibiotic therapy (days) | 1 [1-2] | 1 [1-2] | 1 [0.75-1] | 0.047 |
| Presence of Purpura | 13/67 (19%) | 8/59 (14%) | 5/8 (63%) | 0.004 |
| Septic Shock | 42/67 (63%) | 34/59 (58%) | 8/8 (100%) | 0.053 |
| Empirical antibiotic therapy with Ceftriaxone | 58/67 (87%) | 51/59 (86%) | 7/8 (88%) | 1.000 |
| Steroid therapy | 56/67 (84%) | 49/59 (83%) | 7/8 (88%) | 1.000 |
| IgM enriched Immunoglobulin therapy | 24/67 (36%) | 23/59 (39%) | 1/8 (13%) | 0.283 |

Table 1 Clinical characteristics, therapy and outcomes of study population and comparison between overall survival and overall death

Conclusions. Since IgM enriched Immunoglobulin use is the only protective factor with respect to patients' outcome it could be suggested as a complementary therapy to antibiotics and corticosteroids. A randomized controlled trial is necessary to confirm these data.