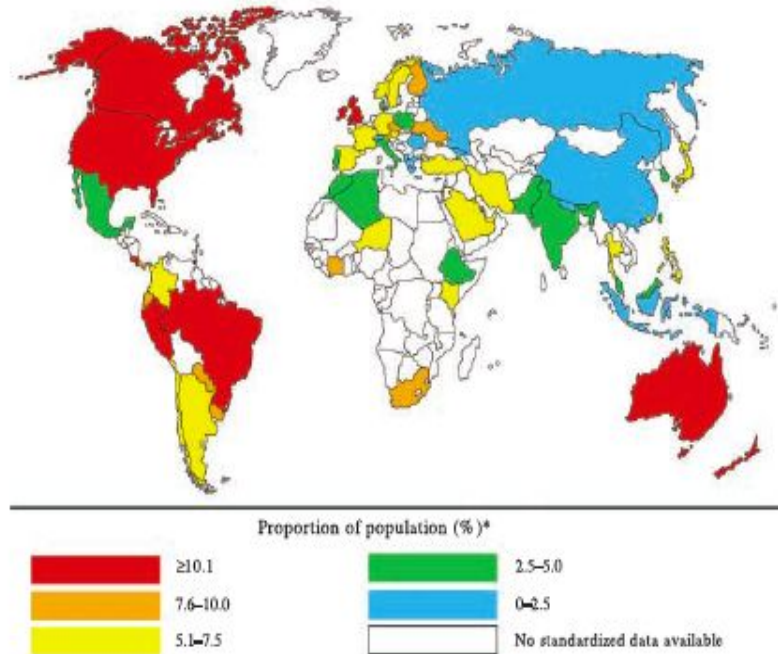# I LIVELLI DI LATTATO COME PREDITTORI DI GRAVITÀ DELL'ASMA ACUTO IN PRONTO SOCCORSO

De Vuono S, PhD MD, Settimi L, MD, Berisha S, MD, Cianci P, MD, Parretti L, MD, Batori G, MD, Vannocchi L, MD, Groff P MD,

XIII congresso nazionale

**simeu**
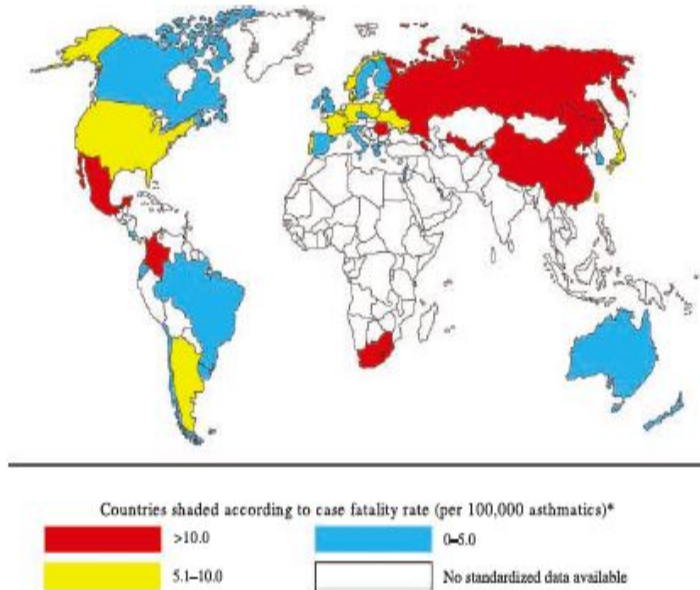
GENOVA 30 MAG - 1 GIU 2024

# Introduction: asthma prevalence



**ITALY 4,5%**

*Masoli et al. Allergy 2004: 59: 469–478*

# Introduction: asthma case fatality rates

| | | | |
|---|---|---|---|
| China | 36.7 | Germany | 5.1 |
| Russia | 28.6 | Spain | 4.9 |
| Uzbekistan | 27.2 | South Korea | 4.9 |
| Albania | 20.8 | Czech Republic | 4.8 |
| South Africa | 18.5 | Israel | 4.7 |
| Singapore | 16.1 | New Zealand | 4.6 |
| Romania | 14.7 | Costa Rica | 3.9 |
| Mexico | 14.5 | Australia | 3.8 |
| Malta | 11.6 | Republic of Ireland | 3.6 |
| Colombia | 10.9 | Italy | 3.6 |
| Denmark | 9.3 | | |
| Ukraine | 8.7 | England | 3.2 |
| Japan | 8.7 | Scotland | 3.0 |
| FYR Macedonia | 8.2 | Estonia | 3.0 |
| Belgium | 7.7 | Wales | 2.9 |
| Latvia | 7.1 | Austria | 2.6 |
| Norway | 7.1 | Ecuador | 2.3 |
| Switzerland | 7.0 | Greece | 2.1 |
| Portugal | 6.9 | Uruguay | 2.1 |
| Poland | 6.6 | Sweden | 2.0 |
| France | 6.5 | Brazil | 1.8 |
| Thailand | 6.2 | Canada | 1.6 |
| Argentina | 5.8 | Finland | 1.6 |
| Hong Kong | 5.6 | Cape Verde | 0.0 |
| United States of America | 5.2 | | |

Countries shaded according to case fatality rate (per 100,000 asthmatics)*

- >10.0
- 5.1–10.0
- 0–5.0
- No standardized data available

## ITALY 3,6%

*Masoli et al. Allergy 2004: 59: 469–478*

# Introduction:
## criteria for categorizing the severity of asthma exacerbations

**The assessment of the severity of acute asthma in the Emergency Department (ED) is difficult and imprecise due to both lack of objective measures of disease severity and variability of signs and symptoms presentation**

| | Mild | Moderate | Severe | Subset: Respiratory Arrest Imminent |
|---|---|---|---|---|
| **Symptoms** | | | | |
| Breathlessness | While walking | While at rest (infant—softer, shorter cry, difficulty feeding) | While at rest (infant—stops feeding) | |
| | Can lie down | Prefers sitting | Sits upright | |
| Talks in | Sentences | Phrases | Words | |
| Alertness | May be agitated | Usually agitated | Usually agitated | Drowsy or confused |
| **Signs** | | | | |
| Respiratory rate | Increased | Increased | Often > 30/minute | |
| | | Guide to rates of breathing in awake children: | | |
| | | Age          Normal rate | | |
| | | < 2 mo        < 60/min | | |
| | | 2–12 mo       < 50/min | | |
| | | 1–5 yr        < 40/min | | |
| | | 6–8 yr        < 30/min | | |
| Use of accessory muscles; suprasternal retractions | Usually not | Commonly | Usually | Paradoxical thoracoabdominal movement |
| Wheeze | Moderate, often only end expiratory | Loud; throughout exhalation | Usually loud; throughout inhalation and exhalation | Absence of wheeze |
| Pulse/minute | < 100 | 100–120 | > 120 | Bradycardia |
| | | Guide to normal pulse rates in children: | | |
| | | Age          Normal rate | | |
| | | 2–12 mo       < 160/min | | |
| | | 1–2 yr        < 120/min | | |
| | | 2–8 yr        < 110/min | | |
| Pulsus paradoxus | Absent < 10 mm Hg | May be present 10–25 mm Hg | Often present > 25 mm Hg (adult), 20–40 mm Hg (child) | Absence suggests respiratory muscle fatigue |
| **Functional assessment** | | | | |
| PEF percent predicted or percent personal best | ≥ 70 percent | ~ 40–69 percent or response lasts < 2 hours | < 40 percent | < 25 percent (Note: PEF testing may not be needed in very severe attacks) |
| $Pa_{O_2}$ (on air) | Normal (test not usually necessary) | ≥ 60 mm Hg (test not usually necessary) | < 60 mm Hg: possible cyanosis | |
| and/or | | | | |
| $Pco_2$ | < 42 mm Hg (test not usually necessary) | < 42 mm Hg (test not usually necessary) | ≥ 42 mm Hg: possible respiratory failure | |
| $Sa_{O_2}$ percent (on air) at sea level | > 95 percent (test not usually necessary) | 90–95 percent (test not usually necessary) | < 90 percent | |
| Hypercapnia (hypoventilation) develops more readily in young children than in adults and adolescents. | | | | |

*Carlos A et al. PROCEEDINGS OF THE AMERICAN THORACIC SOCIETY VOL 6 2009*

# Aim of the study

**Identify the possible predictors of acute asthma severity in the**

**Emergency Department**

# Materials and methods

**We retrospectively enrolled 62 subjects referred to our ED for acute asthma**

**Study period: 1s$^t$ January 2023-31$^{th}$ March 2024**

**Comorbidities considered:**
- **Pneumonia**
- **Allergic diathesis**
- **Cancer**
- **PAOD**
- **HTN**
- **DM**
- **AF**
- **CAD**
- **COPD**
- **Smoke**

**At emergency room arrival the following data were collected:**
- **Clinical medical history**
- **Vital parameters**
- **Laboratory data**
- **Blood gas analysis**

**We also assesed if subjects assumed beta-2 agonist, steroids and antibiotics before arrival to the ED**
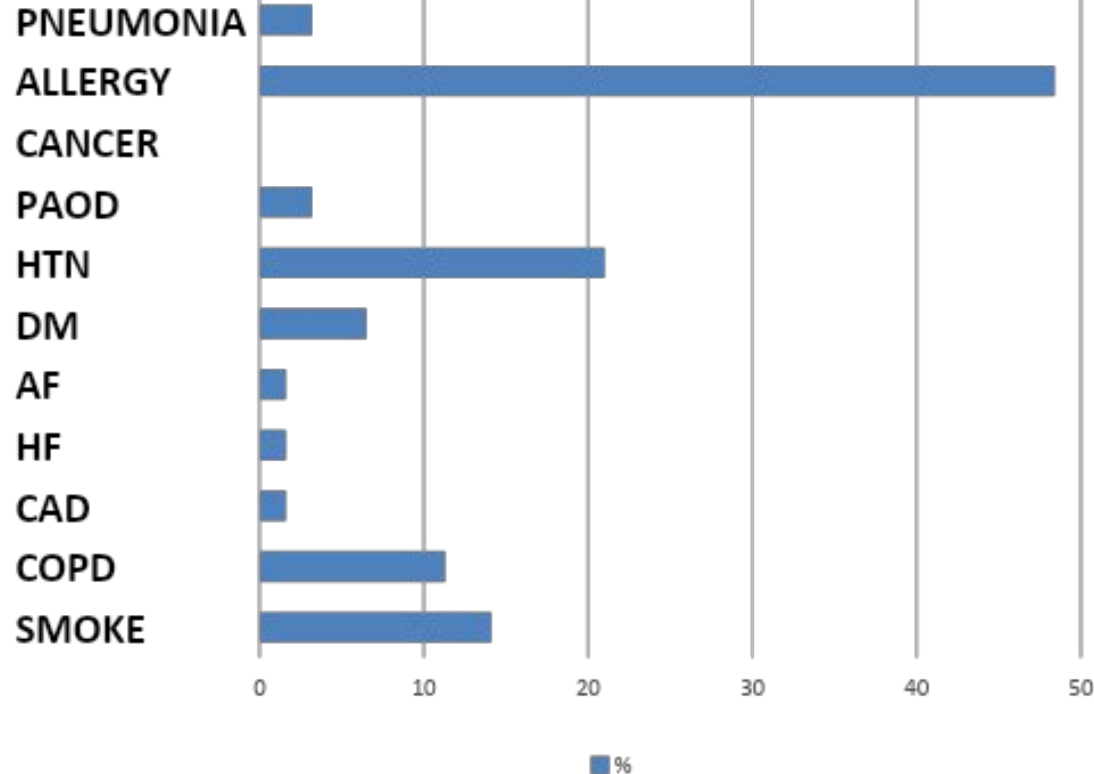
**END-POINT: IN-HOSPITAL ADMISSION**

# Results: general characteristics of the population

GENDER

58% Females
42% Males

Males | Females
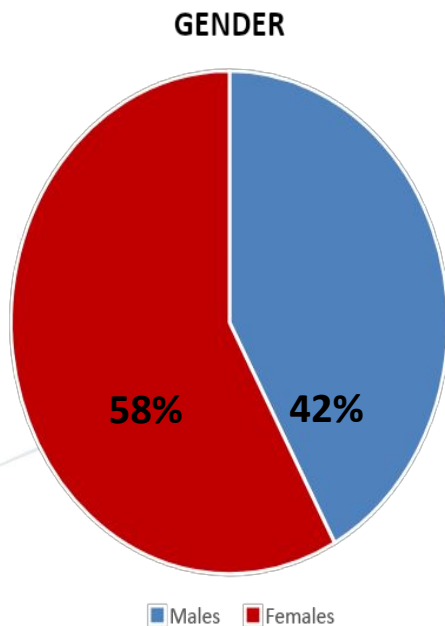
| | Mean | SD (±) |
|---|---|---|
| Age, *years* | 43 | 18 |
| MAP, *mmHg* | 99 | 12 |
| HR, *bpm* | 85 | 14 |
| pH | 7.41 | 0.4 |
| P/F | 322 | 74 |
| $PaCO_2$, *mmHg* | 38.6 | 6.1 |
| $HCO_3^-$, *mmol/L* | 24.7 | 2.6 |
| Lactates, *mmol/L* | 1.17 | 0.7 |
| WBC, $10^3/mm^3$ | 10.7 | 3.7 |
| Hb, *g/dl* | 14.3 | 1.6 |
| Creatininemia, *mg/dl* | 0.8 | 0.2 |
| GFR, ml/min/1,73 m$^2$ | 104 | 21 |
| CRP, *mg/dl* | 1 | 1.5 |

# Results

**Percentage of comorbidities in the population**



**Therapy assumed before ED admission**
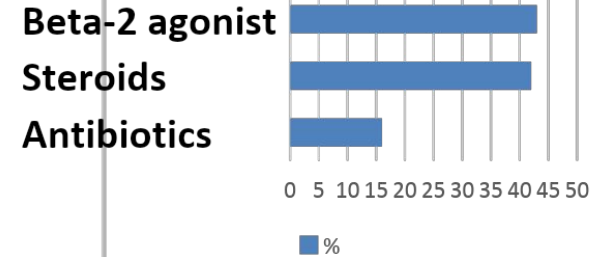


**27/62 (43,5%) required in-hospital admission**

# Results

## Comparision between subjects discharged from the ED (group 1) and hospitalized subjects (group 2)

| | GROUP 1 | GROUP 2 | *p* |
|---|---|---|---|
| Age, *years* | 40,2 ± 17 | 46,5 ± 19 | ns |
| MAP, *mmHg* | 101 ± 10 | 96 ± 13 | ns |
| HR, *bpm* | 87 ± 11 | 83 ± 17 | ns |
| pH | 7.41 ± 0.04 | 7.41 ± 0.04 | ns |
| **P/F** | **365 ± 61** | **280 ± 60** | **<.001** |
| PaCO$_2$, *mmHg* | 38.7 ± 5.2 | 38.5 ± 6.9 | ns |
| HCO$_3^-$, *mmol/L* | 24.7 ± 1.7 | 24.8 ± 3.2 | ns |
| **Lactates, *mmol/L*** | **0.85 ± 0.4** | **1.4 ± 0.8** | **.003** |
| **WBC, *$10^3/mm^3$*** | **9.7 ± 3.1** | **11.8 ± 4.1** | **.027** |
| Hb, *g/dl* | 14.3 ± 1.6 | 14.3 ± 1.6 | ns |
| Creatininemia, *mg/dl* | 0.8 ± 0.1 | 0.8 ± 0.3 | ns |
| GFR, ml/min/1,73 m$^2$ | 105 ± 21 | 103 ± 21 | ns |
| CRP, *mg/dl* | 0.6 ± 0.7 | 1.5 ± 2.1 | ns |

| | NO BETA-2 agonist | BETA-2 agonist | *p* |
|---|---|---|---|
| Lactates, *mmol/L* | 1,05 ± 0,7 | 1,31 ± 0,7 | ns |

| | GROUP 1 | | GROUP 2 | | p |
|---|---|---|---|---|---|
| BETA-2 AGONIST | Y | 13 | Y | 13 | ns |
| | N | 22 | N | 14 | |
| STEROIDS | Y | 12 | Y | 14 | ns |
| | N | 23 | N | 13 | |
| ANTIBIOTICS | Y | 4 | Y | 6 | ns |
| | N | 31 | N | 21 | |

| | GROUP 1 | | GROUP 2 | | p |
|---|---|---|---|---|---|
| Gender | M | 15 | M | 11 | ns |
| | F | 20 | F | 16 | |
| Smoke | Y | 3 | Y | 6 | ns |
| | N | 32 | N | 21 | |
| Allergic diathesis | Y | 4 | Y | 6 | ns |
| | N | 31 | N | 21 | |

# Results

| | OR | 95% IC | p |
|---|---|---|---|
| GENDER | 0.917 | 0.331-2.538 | .867 |
| AGE | 1.020 | 0.991-1.050 | .174 |
| MAP | 0.964 | 0.920-1.010 | .122 |
| HR | 0.980 | 0.943-1.018 | .292 |
| SMOKE | 3.048 | 0.686-13.539 | .143 |
| **P/F** | **0.967** | **0.948-0.987** | **.001** |
| PH | 1.412 | 0.000-881074 | .960 |
| $PaCO_2$ | 0.996 | 0.906-1.095 | .936 |
| HCO3 | 1.012 | 0.810-1.264 | .918 |
| **LACTATES** | **7.441** | **1.561-35.458** | **.012** |
| HB | 0.979 | 0.751-1.340 | .894 |
| **WBC** | **1.184** | **1.013-1.383** | **.033** |
| CREATININEMIA | 1.037 | 0.095-11.368 | .976 |
| GFR | 0.996 | 0.972-1.020 | .743 |
| CRP | 1.862 | 0.960-3.610 | .066 |

**Univariate correlations between the variables included in the study and in-hospital admission**
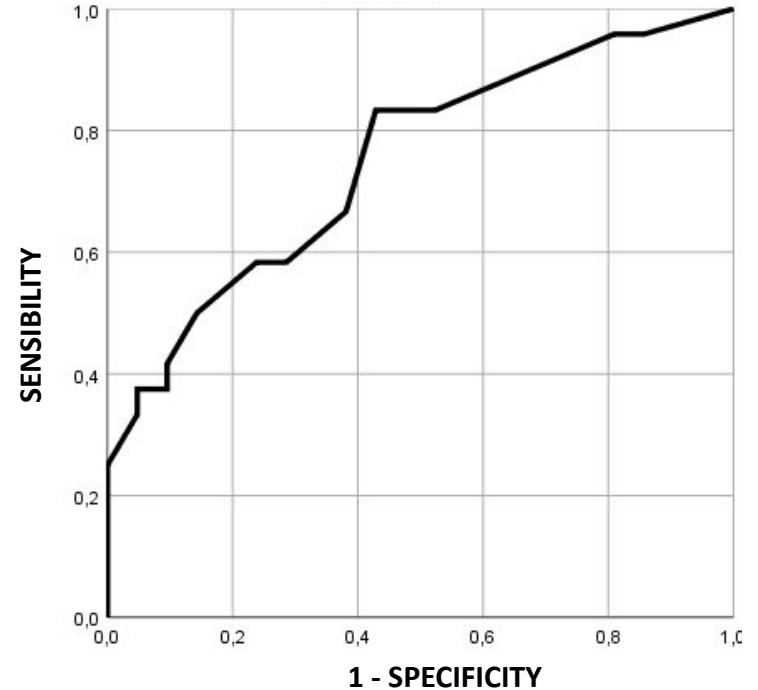
**Multivariate analysis (in-hospital admission)**

| | OR | 95% IC | p |
|---|---|---|---|
| **LACTATES** | **9.190** | **1.042-81.038** | **.046** |
| AGE | 1.003 | 0.955-1.052 | .914 |
| **P/F** | **0.914** | **0.939-0.989** | **.005** |
| WBC | 1.116 | 0.883-1.495 | .463 |

# ROC CURVE

**LACTATE LEVELS AND NEED FOR IN-HOSPITAL ADMISSION**

**AUROC of 0.740**

**CUT-OFF 0,850 mmol/L: Sensibility 83%, Specificity 57%**

# Discussion

**Results of our study suggest that lactate levels detected at the time of admission to the ED in subjects with acute asthma may be an independent predictor of a greater probability of being hospitalized and therefore of the severity of the acute**

- The prevalence of hyperlactatemia in asthma exacerbation is much more frequent than previously estimated.

- Two prospective observational studies involving adults and children with acute asthma in the emergency setting found that between 50% and 80% of patients presented with hyperlactatemia.

- Data correlating increased lactates to prognosis have been questioned by a dynamic increase secondary to increased SABA assumption

- Despite these findings, the pathophysiology and clinical significance of this phenomenon remains controversial.

**Box 1   Causes of lactic acidosis. Modified from Doddo and Spiro.[2]**
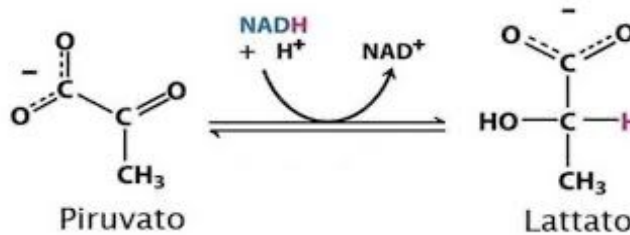
Type A lactic acidosis
  Global hypoxia
  Hypoperfusion/ischaemia/shock
  Local ischaemia
  Severe asthma or chronic obstructive pulmonary disease
  Cardiopulmonary arrest
  Carbon monoxide poisoning
Type B lactic acidosis
  Drugs
  Metformin
  Catecholamines
  Isonicotinylhydrazine
  Ethylene glycol
  Salicylates
  Nucleoside reverse transcriptase inhibitors
  Alcoholic and diabetic ketoacidosis
  Thiamine deficiency
  Large fructose loads
  Increased muscular effort
  Renal/hepatic failure
  Inborn errors of metabolism (pyruvate dehydrogenase deficiency)
  Malignancy
  Seizures
  Cyanide poisoning

*Rodrigo J et al. CHEST / 145 / 1 / JANUARY 2014; Lau E, et al. BMJ Case Rep 2013*

# Discussion

## Hyperlactatemia in asthma exacerbation



Catecholamine and/or respiratory alcalosis
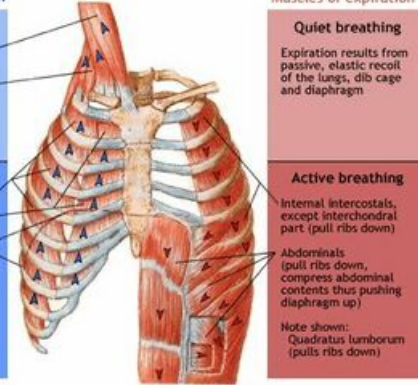
# Conclusions

- **The assessment of the severity of acute asthma in the Emergency Department (ED) is difficult and imprecise.**

- **Arterial lactate levels measured at the arrival to the Emergency Department may help in predicting the severity of asthma exacerbation.**

- **Hyperlactatemia is frequent during acute asthma, but the underlying pathophysiological mechanisms and its clinical implications are not understood.**

- **Further larger and prospective studies are needed.**