

# Prematurity and Sepsis - Features and Approach Difficulties During Neonatal Emergency Transfer

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**ABSTRACT:** Purpose - We aimed to identify conditions, means and methods of suspecting, certification and stratification of neonatal sepsis, to prioritize and define levels of management during evacuation, and to follow the neonatal sepsis succeeding the transfer. Material and method - An observational study was conducted between 1 January 2011 – the 1 January 2015, that included 610 preterm newborns with suspected sepsis transferred by UTIM NN or HEMS Craiova. We statistically studied confirmation rate of suspected sepsis, the sepsis onset condition, severity stratification, and correlate with medical centers performance assisting newborns and planning transfers. A follow up performed two weeks after evacuation. Results - We detected low rate of detection and affirmed sepsis: n=38 (6.25%) - C.I. (95%): 4.454309335 and very high level of founded unsuspected sepsis: n=85 (13.98026316%) C.I. (95%): 4.982552268, 9 of them being very low body weight newborns (1.480263158%). High rate of founded, unaffirmed respiratory distress 23.35526316% (n=142), C.I. (95%): 5.383960957, as sign of sepsis. High rate of accidental hypoglycemia/hypothermia founded by emergency evacuation team: n=131 (21.54605263%), especially to VLBW newborns, associate with sepsis, respiratory failure or confounding with. Conclusions - Newborns transfer its self generates multiple additional risks, including sepsis, but not neglected any stress generated by transport conditions, so that „in utero” transfer has to be extended in current practice for high risk fetus, mother or special medical conditions to limit newborns transfers. Wider use of telemedicine would facilitate refining the transfer criteria.

**KEYWORDS:** neonatal sepsis, preterm newborne, newbornes transfer protochol, medical air evacuation, in – utero transfer, telemedicine

## Introduction

Newborn's sepsis represents a significant cause of neonatal mortality, particularly in vulnerable groups, and emergency medicine physician and its prehospital care unit is often asked to transfer newborns with sepsis. Although patients at high risk groups are specified, risk stratification is less defined, but constantly, prematurity involved.

## Purpose

The purpose of this study is represented on the one hand by identifying the conditions, means and methods of suspecting and early neonatal sepsis certification especially in premature newborn, severity stratification, transfer priority and recommended levels of management during neonatal emergency evacuation.

The second objective of the study was to follow the exact extent of neonatal sepsis succeeding the transfer of prematurely newly-

born, so that we can propose ways to minimize the complications.

## Material and method.

The group of study consisted in 610 preterm newbornes from Romania South - Western region of development OLTENIA, transferred by ground newborns mobil intensive care unit (UTIM NN) or HEMS Craiova between 1 January 2011 – the 1 January 2015. Both structures operates as a medical prehospital teams of Emergency Department of Emergency Hospital Craiova. ED - SMURD Craiova is a regional directing operational and decisional echelon for newborns transfer and newborns department of Emergency Hospital Craiova is a level II B medical center for newborns.

Inclusion criteria for the study – only prematurely newborns transported from the region enrolled. Only the newborns

evacuated by SMURD Craiova (ICU ground or HEMS unit) analyzed.

The main affirmed reason as a request criteria for newborn s mobil ICU team considered.

The Romanian S- W development region the IV th - Oltenia, include 5 county with approximately 2,5 mil. peoples: Valcea, Dolj, Gorj, Olt, Mehedinti. Each of this county has a county hospital with include or separate maternal department – level II a center, except University Emergency County Hospital Craiova. There are in Craiova several other different level hospitals having compartments of gynecology and obstetrics level I, II a. The national reference level III centers are in Bucharest hospitals (Marie Curie Hospital and Grigore Alexandrescu Hospital).

Distances between Craiova with any of the others centers are maximum 130 km.

The coordination of missions realized by Bucharest national dispatch ELI – newborns, in cooperation with Târgu Mures national dispatch ELI – newborn’s. Each of these coordinates the regional HEMS and ground newborn’s units, such SMURD Craiova.

For each of patient we statistically analyzed several aspects of transfer criteria, evacuation delay, delivery context and conditions, gestational age and weight of newborns, some specific items of cases that influenced the case evolution, preparedness of the transfer related to the level of the sending and receiving centers and to severity of newborns condition, flight parameters for HEMS evacuation, number and conditions of serial evacuation, evolution of newborns following the transfer (within 5 days).

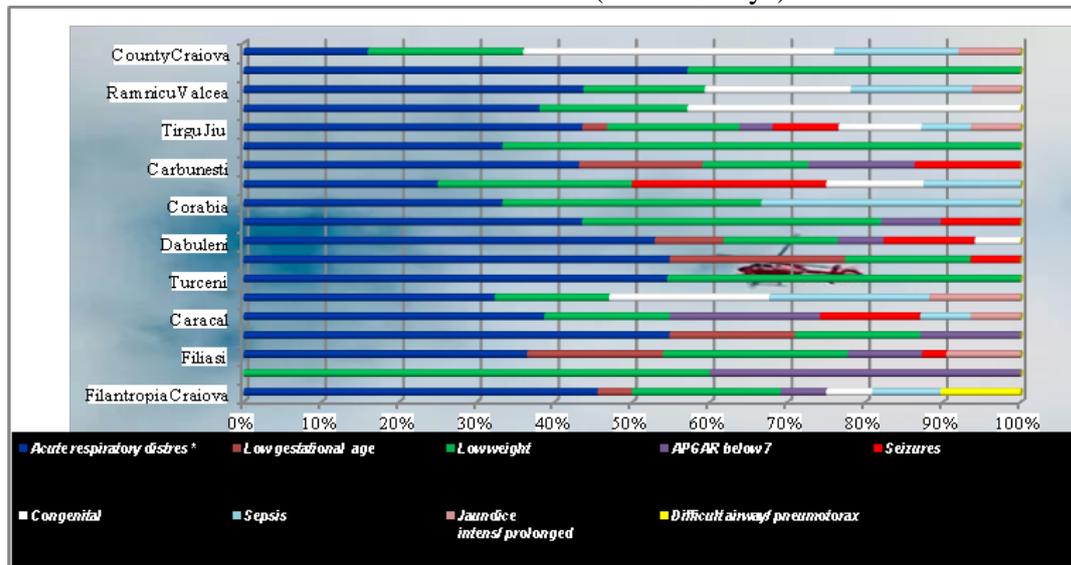


Fig.1. The main medical reasons for medical transfer request (\*or similar - high respiratory rate, high respiratory effort, cyanosis, dyspnea, apnea episodes)

## Results

We directed the first analysis to identify the main medical reasons for requesting a mobile intensive care and neonatal transport unit for an emergent medical evacuation (Fig.1)

Data analysis conduct to the first conclusion that sepsis (n=36) and low weight newborns (n=95) generated 21,46% % of transfer reasons, but in fact, based on newborns transportation teams in scene findings, the cumulate criteria related to sepsis, prematurity / low weight reached to 73,29 %.

In group of the premature and very low body weight (VLBW) newborns without declared sepsis but more than 30h delay of transfer request (n=48), associate sepsis signs or “RED FLAG” RISK FACTORS for Early Onset Sepsis [1] founded to 41 patients, representing 85,41%.

For this group at least one predisposing or precipitating factor of sepsis confirmed: field delivery, premature rupture of membranes, meconium aspiration syndrome, immediate resuscitation required, maternal to fetal infection, so sepsis was not an unexpected event, but an foreseeable one.

Only very few cases presented unexpected associated situations, as confirmed congenital problems (heart/great vessels disease, digestive/urinary tract malformations, Pierre Robin syndrome (n=1), most of the rest being under observation various period of time before delivery, and some of these difficult condition for the newborn being possible to evaluate. The conclusion is that „in utero transfer” value has been serious and constantly underestimated in most cases, and delivery accepted even the low level of the newborns center recognized [2,3] .

The increased deterioration risk as follow: increased rate or respiratory effort / mechanical ventilation required (even not established), multiple attempts of vascular access, artificial nutritional support, hypoglycemia, hypothermia, all of these, equally predictable.

Serial transfers of the patient. A significant number of these patients (n=51) previously transferred between level III and IV hospitals to higher but not appropriate centers (between 42 minutes and 16hours) for different reasons, before the transfer to reference centers.

It is important to note that initially transfer has been made usually with ordinary ambulances, without incubator (12 of these transfers performed in the winter) and in 34 cases with B2 type ambulance (nurse only), before the secondary evacuation mobile newborns ICU team requested (in 27 cases HEMS).

We identified 24 others newborns (3, 93% of patients) for which, transfer request criteria (time and destination centers) has been chosen for non medical reasons, as parental home proximity or parental request, at long distance ( over 300 km – over 3 hours transportation).

All of these patients developed sepsis between 18 – 36 hours from transfer, even 3 at term newborns with minor risk criteria (average weight) but serial transfers. [4].

A series of circumstantial elements identified in different transfer situation:

Delay of the transfer request face to the deterioration rhythm of the patient is difficult to appreciate due to uncertainty localization in time of onset and rate of worsening condition, for the newborns in critical condition. For the patients transferred to punctual elements persistent over time (lower of 7 APGAR scale, weight or gestational age) transfer request expediency varied enormously, with limits between 10 minutes and 29 hours.

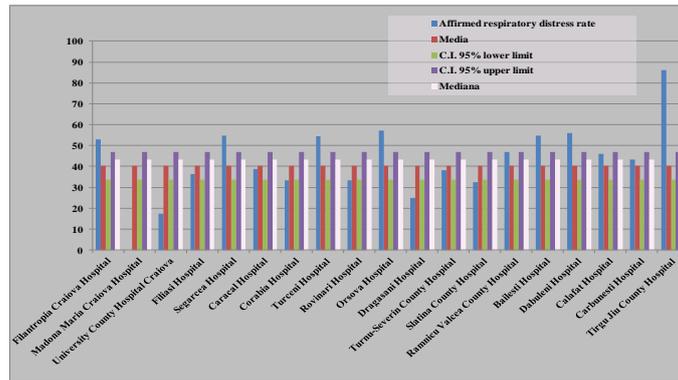
Both extremes, hasty evacuation of healthy newborns with rapid and favorable adaptation or very long delay without reasonable reasons (such as a very advanced management or complex investigation) were both found in level III and IV hospitals. The exception created by level II medical center Târgu Jiu County Hospital, which both rate and delayed transfers of the precipitates is above the lower levels hospitals, a total of 13 patients transferred for malformations, lower of 7 APGAR scale, weight or gestational age), for 4 of them advice transfer was requested 1 hour after birth, 6 of them in more than 18 hours of birth, with a maximum of 42 hours days (anal - rectal malformation). Average time of transfer request was 11ore and 12 minutes for such patients.

Another issue examined was the correlation between the founded patient condition and the affirmed patient condition at the transfer request moment (Fig.2a-c).

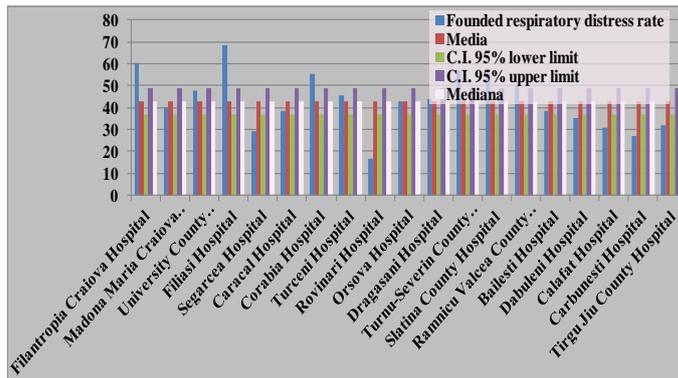
Even though the respiratory distress are so frequently accused as transfer criteria, a lots of confusion are persisting in its identification. From 262 patients transferred for affirmed respiratory distress as the main transfer reason (N =610, 43.09%) median: 40.24, STDEV: 14.85, C.I. (95%): 6.687, but only 127 confirmed (concordance diagnosis -44.24%).

In the same time, founded respiratory distress confirmed in place by the evacuation time, as respiratory effort, retraction or toraco – abdominal balance (percentile values) are very high: n=142 (23.35%), maximum value: 68.25, median: 42.91, STDEV: 13.023, C.I. (95%): 5.85, and founded, unsuspected respiratory distress increasing to maximum value: 45.455, median: 26.21, C.I. (95%): 5.38, STDEV: 11.97. For example, to the 12 patients with other pathological elements reported we identified major life threatening elements (6 severe respiratory distress – 3 of them related aspiration syndrome [5], 2 left minimum pneumothorax to patients transferred for fractured clavicle, 2 compressive pneumothorax, and 2 patients with malpositions of the tracheal tube - 1 selective intubation of the right bronchus and 1 esophageal intubation). They represented 5,47% of cases.

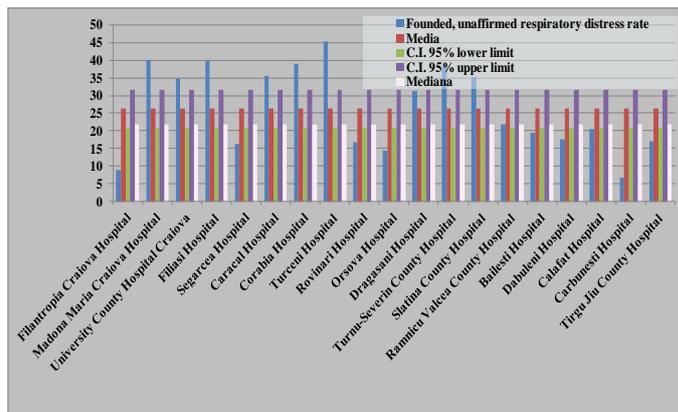
In the same time a series of 13 patients finally interpreted as transient tachypnea in very low body weight condition, none of pathological condition confirmed. Evacuation, for them, has been not only useless, but a predisposing, risk factor for sepsis.



a. Affirmed respiratory distress (percentile values)



b. Founded unsuspected, unaffirmed respiratory distress (percentile values)



c. Founded, unsuspected, respiratory distress to VLBW newborns (percentile values)

Fig.2.a-c Confirmed findings related to affirmed transfer reasons

It is also interesting to note that the accuracy of diagnosis of this syndrome was well below to some level II hospital with newborns care department and ICU facilities for that (Târgu Jiu - 36.36%). Some level III and IV hospitals have a much higher accuracy (Filantropia Craiova Hospital - 100%, Filiasi - 77.77%, Cărbunești - 46.66%). Even excluding these hospitals, the results for the level III and IV centers is significantly close to the general average (40.47%). There are a number of hospitals in which no cases were reported as respiratory distress - confirmed (Turceni and Rovinari, but

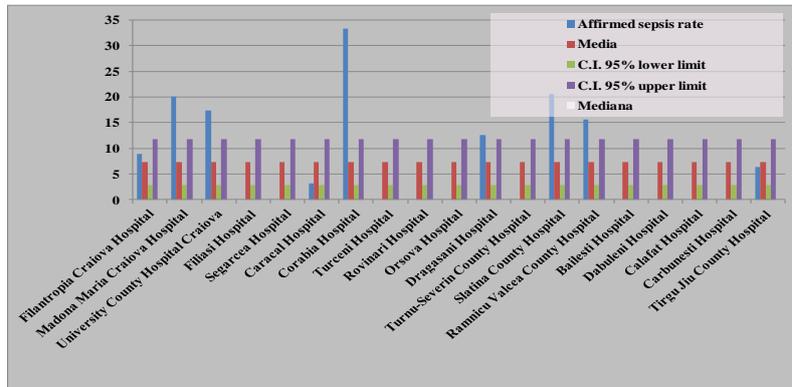
the interpretation is inconsistent because of the small number of cases.)

For sepsis (Fig.3a-c) confirmation the rate of recognition or suspicion are even lower, only 2 centers having confirmed reports as a request criteria. [6,7,8]. We determined a surprising low rate of affirmed sepsis, as main transfer request criterion: n=38 (6.25%) median: 7.25, C.I. (95%): 4.45, STDEV: 9.906

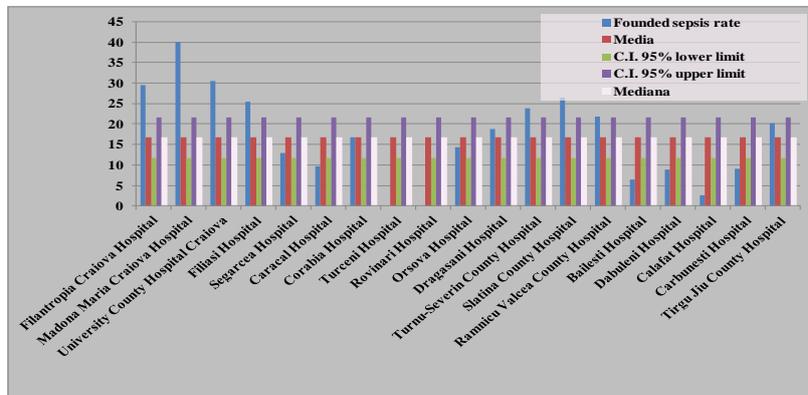
Actually, a high rate of sepsis founded in scene by the transfer teams: n=109 (17.92%) - median: 16.67, STDEV: 11.08, C.I. (95%): 4.98, so, founded, not suspected sepsis: n=85 (13.98

6%) – maximum value: 25.39, median: 12.15, STDEV: 7.35, C.I. (95%): 3.30. For VLBW newborns founded, not suspected sepsis: n=9 (1.48%) - median: 1.26, STDEV: 2.13, C.I. (95%): 0.96. That confirms the supposition that

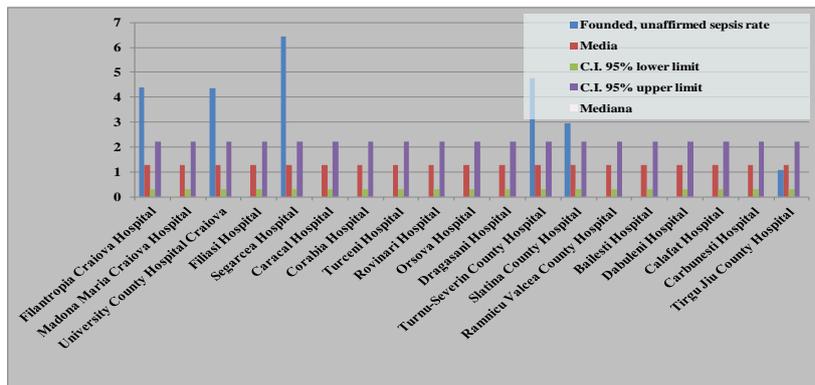
a lots of initial manifestation of sepsis are ignored by the unspecialized physicians, confounding with difficult adaptation, generating progressive deterioration before becoming visible.



a. Affirmed sepsis rate



b. Founded unsuspected, unconfirmed, undetected sepsis rate



c. Founded unsuspected, unconfirmed, undetected sepsis rate to VLBW

Fig.3.a-c Confirmation rate of findings associate to sepsis compared to affirmed transfer reasons

As would be expected, some level II hospitals have significantly above average (Slatina County hospital, N= 34 patients, affirmed sepsis: n=7 (20.58%), detected sepsis: n=9 (26.47%), founded, unaffirmed sepsis: n=5 (14.70%): n=1 (2.94%) Ramnicu Valcea County Hospital – N= 32; affirmed sepsis: n=5 (15.625%), founded sepsis: n=7 (21.875%),

founded, unaffirmed sepsis: n=5 (15.625%), founded, unaffirmed sepsis sepsis: n= 0 (0%). The regional center of Craiova University County Hospital has an average line observed by 50%: N= 23, affirmed sepsis: n=4 (17.39%), Founded sepsis: n=7 (30.43%), founded sepsis, unsuspected: n=3 (13.04%), 1 of them being VLBW

7 cases reported as low APGAR were consecutive to cesarean section in general anesthesia conditions, with no reasons to calculate the score immediately. In fact, at newborn s transportation unit arrival 6 patients does not presenting any signs of serious medical problem, being reactive, well looking, and with adequate progressing of adaptation excepting small degree of prematurity. Only one of them has strong indication of transfer because of mother eclampsia (condition for emergency cesarean section), but, again, in „utero transfer” will be a way to solve the case than newborn transportation. The newborn developed a group B streptococcal infection the 4th day after the transfer

A series of 8 patients with suspected cardiac malformation actually showed suggestive clinical elements of acute respiratory distress (cyanosis, tachypnea, increased respiratory effort).

If this information is added to the above, it appears that the combined rate of inconsistencies between diagnostic elements requesting transfer to those found on scene, in this group exceeds, for this diagnostic group, 75% either undervaluation or overvaluation that.

It is important to note from the above data that the difference in classification level of the hospital does not accurately reflect the level of the case medical data collection and submission, and this affects the quality of the decision on the type of means of evacuation.

For a series of 5 patients prolonged jaundice, wrongly, was not interpreted as a sign of sepsis, only 1 patient had biliary tract malformation.

A number of 23 patients reported as seizures and acute respiratory distress has been found with hypoglycemia this being in fact the actually cause of altered status to these patients, amended by correcting blood glucose at transfer team arrival moment.

In 127 cases - Fig.4 - (21.54%, N=610), maximum value: 57.14, median: 26.044, STDEV: 16.72, C.I. (95%): 7.52 reported as acute respiratory distress, taken from level II to IV centers, the patients were hypothermic (n= 8, even severe, 31,3C degree in 1 case, in total representing 1,47% of cases), and 1 other case were overheated (presenting high respiratory rate and dehydration) or hypoglycemic. On 3 separate cases dehydration were identified, caused by incorrect rate of fluid administration.

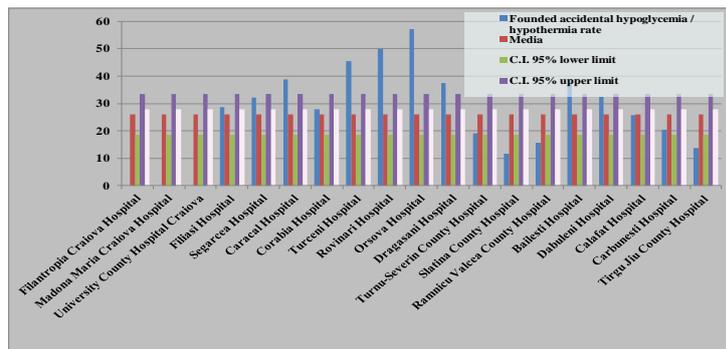


Fig.4 Founded metabolic disorders rate (hypoglycemia / hypothermia)

For a total of 98 patients (16,07%) did not confirmed any element of serious or acute deterioration, persistent or severe to justify the emergency transfer request.

Related to the seriousness of the newborn condition we analyzed the level of patient’s preparation in line with transfer guidelines [3]:

It was not always revealed a vital management and investigative functions consistent with the level of seriousness announced. 10 patients were intubated prior to resuscitation and transfer unit arrival (4 of them from Slatina Hospital and 6 of them from Filantropia Craiova Hospital). Another one was

intubated but declared dead before arrival team (Turnu Severin County Hospital).

Only for 11 patients with affirmed respiratory or congenital problems a chest x Ray performed, despite chest x Ray recognized as the most valuable method for recognizing the 5 most common causes of newborn s respiratory distress: hyaline membrane disease, bronchopulmonary dysplasia, transient tachypnea of the newborn, meconium aspiration syndrome, neonatal pneumonia. [9,10,11]

Only for 8 patients a chest and abdomen ultrasonography performed, despite a number of congenital pathology affirmed and beneficial

lung findings for the diagnosis of severe neonatal pneumonia. [12,13]

Only to 10 patients an EAB determination provided. [1]

Only 202 patients had an effective vascular access in place.

None blood culture, presepsin or hCRP determination [1] performed before evacuation.

Only 38 patients with antibiotic prophylaxis [1,8]

Under these situation, a series of 11 patients in critical condition required complex advanced life support maneuvers to putting in optimal or at least stable evacuation condition. We practiced, 22 tracheal intubations (19 of them with general anesthetic induction), 6 chest drainage, a number of 397 intravenous peripheral access, 5 central access – femoral, 14 intra osseous access and 5 umbilical vein catheterization to a critical patients with no patent airway or functional vascular access in place.

For 12 patients controlled ventilation established, 35 patients noninvasive ventilated and for 10 patients assisted ventilation decided.

We decided and applied inotropic support to 13 severe septic shock patient, and complex acid base and electrolytic rebalancing based of ASTRUP determination for 38 patients.

7 upper gastrointestinal tube were placed.

A number of 5 patients required resuscitation (one of them including during air evacuation) because of the severity of its condition, one of them declared dead on scene after prolonged resuscitation.

The final results - one died during transfer, one newborn died before resuscitation team arrival, one died after the resuscitation team arrival on scene and after advance resuscitation procedures were practiced (the transfer was cancelled)

Of these, only 3 patients were initial announced with these severity elements these special needs and requesting air medical evacuation (County Hospital Craiova for Bucharest centers).

## Discussions

Common in premature newborn, especially very low weight and extreme prematurity, sepsis represents a developing, predictable complication, ubiquitous in levels I-II newborns level centers.

The main two complex circumstances consist of polymorphism for the onset and the

difficulties of interpreting the evolutionary clinical and paraclinical findings.

Often, their onset are represented by the elements of hypoxemia associate to compensatory tachypnoea (and increased respiratory effort), which are undervalued or wrongly interpreted, only pulsoximetry being monitored, but not relevant.

Digestive disorders-specific associated to development of serious sepsis are often confused with primary digestive pathology

Oligoanuria related sepsis is often confused with late installation of diuresis.

Presepsin levels do not correlate at all with the severity of sepsis, as things happen in adults. The same situation about biomarkers of miocardial injury related sepsis, but CRP >20mg/L or rising quickly and positive blood culture are valuable but rarely used instruments to confirm sepsis.

Evan for these, delayed case study on sepsis biomarkers (performed into the reference centers) was completely confusing, showing both: discordant level of presepsin with general clinical and paraclinical signs and non specific level progressive correlation in septic confirmed context. So that the point of care determination showed in 13 cases very high levels (highest than 6000 units) to newborns with little stages of sepsis but no septic shock. In the same time to 8 cases of severe sepsis the dynamic level of presepsin, during a week, did not register significant changes likely to be used as a predictive element (maintaining high values independent of the sepsis evolution).

In this condition, the MEDS score and MODS score calculators being not applicable to newborn, the risk evaluation and stratification for sepsis in absence of emergency lab, imaging and extensive monitoring has been established only on the unexplained, rapid deterioration, to a preterm and vulnerable baby. The most useful finding revealed by glycemia instability and arterial blood gases, with both calculated and measured parameters (lactate, pH), applicable equally for ventilated vs. non ventilated patients

Need to assist ventilation is often overlooked until the late stages of respiratory failure, frequently only oxygenation being provided, in excess some times, despite the evidence of positive pressure ventilation and surfactant administration needs. So that, choosing ventilation parameters is a difficult choice, especially for extreme prematurity or advanced stages of sepsis, with increased risks of pneumothorax in case of air evacuation and

relative high altitude (HEMS, 2000 – 3500 feet). [14,15]

Serious underestimation elements is common in small, unspecialized centers, which still uses extrapolation to child deterioration criteria elements from adults. Paradoxically transfer delay is more common in these centers than in more advanced.

Dehydration is underestimated as a factor of aggravation of the condition of the patient, as well as thermal protection. It turns out that a fifth of patients experienced distress elements of vital functions due to metabolic disorders and insufficient standards of care, they having no special medical needs and obviously, no emergency transfer indication whether identifying problems would have been correct.

This leads to a series of precipitated discharges from these centers because of a damages caused strictly by hypothermia but not recognized and amended accordingly.

Exaggerating the elements of gravity to rushing the evacuation in an attempt to prevent a potential patient deterioration is common for level II centers, which transfers unexpected and nondiscriminatory prioritized a number of patients on the basis of generic, case criteria without any specificity (low weight, medium or low APGAR, eventually after caesarean section calculation). At the same time, preparing patients for evacuation is often discordant both the declared gravity of the case and sometimes the real field situation. According to our previously experience with acute coronary syndrome STEMI evacuation program [16], we consider that available, in use telemedicine to these hospitals, could leads a lots of inappropriate transfers be avoided, delayed or better preplanned and prepared, based on rational and reasonable arguments offered by reference centers.

In both cases it is an important point to establish the real hospital level of competence for newborns care, so they find perfectly safe and does not produce excess on their movement to other centers.

## Conclusions

Newbornes transfer, especially of patient with extreme prematurity generates himself multiple additional risks, including the risk of sepsis is the most formidable, but not neglected any stress generated by vibrations, noise, altitude difference (air evacuation-HEMS), repeated handling and exposure, uncontrolable external condition. So that, we believe that can

be a topic of study to what extent, conditions and especially for which types of patients express request of the parents may be a reliable criterion for inter clinical transfer decision. Finally, it is important that serial short term transfers between hospitals, to be eliminated - a correct identification of the most appropriate hospital to the clinical profile and child gravity, regardless of territorial administrative boundaries, and an exhaust means optimal be mobilized at the right time

Reconsidering criteria, timing, preparation and realisation of the new bornes transfer, we have to mandatory setup in-utero transfer, when possible, as the surest way to reduce both the incidence of neonatal sepsis, gravity, the implications on the development of newborne and subsequent transfers risks cascading, sometimes precipitated by aggravating developments, in patients with extreme fragility of the imunologic and metabolic mechanisms and extremely limited capacity to compensate the vital functions depression, especially the birth of premature and, in this connection, the potential risk of sepsis can be avoided.

Wider use of telemedicine would facilitate refining the criteria for transfer, the optimal choice of appropriate timing and crew and directing of fineness management of evacuation, avoiding precursory unnecessary or precipitated transfers with unprepared patient. In this way, it can make additional criteria assimilated key decisional points for choosing the optimal timing, destination, means of transfer and the best team suited to each case

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## Conflict of interests

The authors declare that they have no conflict of interests.

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