**Original article**

Epidemiological and laboratory features of acute enteric infections

*O. Chemych*, *M. Chemych*, *N. Malysch*, *O. Berest*, *O. Suprun*, *D. Svirydenko*

**Abstract:**

*Background:* This work describes etiological structure and statistics for causes of acute enteric infections and salmonellosis in modern conditions. *Method:* It was analyzed the common epidemiologic signs and indices of modern acute enteric infections (AEI), caused by opportunistic microorganisms (OMO), various viruses and salmonella. *Result:* The research also shows the integrative intoxication indicators of causal groups in endogenous intoxication which point to these phenomena being caused by autointoxication at the moment of one’s own cells disruption as well as induced by bacterial endo- and exotoxins. *Conclusion:* The work compares the etiology of AEI on the basis of reviewing their epidemiological attributes, changes in the integrative indication for endogenous intoxication, as well as vectors and causal correlations between hematological and microbiotic indicators.

**Keywords:** acute enteric infections; salmonellosis; epidemiology; integrative intoxication indicators; microbiocenosis; endogenous intoxication.

**Introduction**

Enteric infections are one of the most important health problem. There are registered up to 4.7 million episodes of diarrhea, including 100 000 cases of severe diarrhea, and 1 600 deaths every day all over the world. Approximately 9 % of deaths in children under five years of age are associated with diarrheal infections.

Recently, the etiological structure of acute enteric infections (AEI) has changed significantly. This is due to the constant evolution of bacteria and the involvement in the pathological process of opportunistic microorganisms (OMO) which are presented in the normal intestinal microflora of man, but with various endogenous and exogenous interactions recorded as etiopathogens. AEI, caused by OMO, they are characterized by the same type of intestinal symptoms and arise with decreasing reactivity of the organism, the massivity of the infective dose.

Salmonella is one of the largest medical and biological health problems in most countries of the world. The highest incidence is observed in economically developed countries. The situation is complicated by the fact that salmonella, due to their pronounced biological plasticity, is capable of prolonging persistence in the human body, causing a severe course of the disease.

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1. Oksana Chemych, Sumy State University, department of infectious diseases with epidemiology, Ukraine. Email: o.chemych@med.sumdu.edu.ua
2. Mykola Chemych, Prof., head of infectious diseases with epidemiology department, Sumy State University, department of infectious diseases with epidemiology, Ukraine. Email: n.chemych@kinf.sumdu.edu.ua
3. Nina Malysch Sumy State University, department of infectious diseases with epidemiology, Ukraine. Email: n.malysh@kinf.sumdu.edu.ua
4. Oleh Berest, . Sumy State University, department of computer science, Ukraine. Email: o.berest@cs.sumdu.edu.ua
5. Oleksandr Suprun, Donetsk National Medical University, department of internal medicine, Ukraine. Email: info@kinf.sumdu.edu.ua
6. Diana Svirydenko, student of the medical institute, Sumy State University, department of infectious diseases with epidemiology, Ukraine. Email: info@kinf.sumdu.edu.ua

**Correspondence to:** Oksana Chemych, Sumy State University, department of infectious diseases with epidemiology, Ukraine. Sumy, Rymskogo-Korsakova St. 2 Postal code: 40007. Email: o.chemych@med.sumdu.edu.ua
Features of Acute Enteric Infections

Objective. The objective of this study is to improve the criteria for AEI diagnosis which are caused by bacterial and viral factors, salmonella. This moment of research is based on epidemiologic and laboratory data gathered in periods of infectivity.

Patients and methods. The research is based on examination and analysis of 210 medical records of in-hospital patients with various AEI caused by OMO, viruses and salmonella. The study was carried out in Sumy regional infectious diseases hospital by Z. J. Krasovitsky, where the medical records was for the period from 2014 to 2016. The average age of patients was (41.14±1.20) years.

Every patient was checked via different laboratory evaluations: clinical blood analysis, bacteriologic/virological stool test, serum diagnosis and ELISA (enzyme-linked immunosorbent assay) tests. These check-ups were made in order to define the AEI causes. Besides the common laboratory analyses, all patients underwent a screening of microbiocenosis of colon before the treatment and after (5.76±0.16) days of in-hospital treatments.

All persons whose medical records were used, it was made complete clinical blood analysis via a commonplace method using hematology analyser Cobas Micros; it was studied: absolute white cell count (10⁹/liter), erythrocyte sedimentation rate (mm/hour) and white cell formulae with a following integral indices calculations in the field of endogenous intoxication, such as: leukocyte intoxication index (LII), hematological intoxication index (HII), index of leukocytes shift (ISL), lymphocyte index (Iₖₜₚₚ). The experiment comparison group consisted of 44 intact donors with clean medical record that volunteered of Sumy Regional center of blood banking and transfusiology. The average age of donors was (37.95±1.72) years. The gender basis was absolutely equal – 22 male and 22 female donors.

All data was stored for further review in “Electronic research papers”. Results of clinical trials and conducted research were analyzed by via variation statistics using Microsoft Office Excel 2010, Statistica 10 and an online browser-based calculator for medical data (http://medstatistic.ru/calculators/calchit.html). The methods used in the research include Student’s t-criterion and Pearson’s x²-squared distribution of data.

Ethical clearance: Manuscripts based on the study conducted in accordance to the ethical standards laid down in the 1964 Declaration of Helsinki revised in the year 2000.

Results and Discussion.

It was conducted a set of clinical and laboratory surveys for carrying out the tasks set in work. The observed patients included: 70 infected with AEI caused by OMO and viruses, and 140 infected with salmonellosis, who were being treated at the regional infectious diseases hospital, at their average age was (41.14±1.20) years. All patients were hospitalized for (1.86±0.07) days since time of infection onset.

Depending on the etiology everybody of the surveyed was separated into two groups by the random selection method. The first group consisted of 70 people and the second - 140 people. The group of 70 patients, whose acute enteric infections were caused by opportunist microorganisms, was further separated into 3 sub-groups. AEI-I group where by the cause of infection it was a string of different OMO, included 37 observed, AEI-II KI group with the cause of infection Klebsiella pneumoniae included 22 observed, and the AEI-III Vir group included 11 patients with virus-based etiology. There were 140 patients with salmonellosis who was divided into 2 sub-groups. Just like with AEI, the separation was carried out depending on the cause S-I S. typh. – 43 patients (Salmonella typhimurium) and S-II S. ent. – 97 patients (Salmonella enteritidis).

Females were prevalent among infected with AEI, and men were salmonellosis (p <0.05). Patients suffering with salmonellosis were older on average (43.61±1.49) that AEI patients (36.20±1.92) (p <0.05).

The most common causes for infections were: Klebsiella pneumonia, viruses, E. coli pathogenic infections, Pseudomonas aeruginosae (picture 3). The majority of instances in salmonellosis infection were caused by Salmonella enteritidis (69.0 %), Salmonella typhimurium was detected almost in 2 times less (31.0 %) than Salmonella enteritidis (p <0.01) (figure 1).

The analysis of all observed was conducted in hand with the rising number of new patients incoming to indoor hospitalization since May to August 2016, the maximum count of people was reached in July and August.

The case of big spike in AEI disease count should be pointed out. There were 2 peak rises of hospitalization rates: from February to March (21.3 – 26.5 %) and from July to August (28.0 – 32.7 %).
The salmonellosis infection hospitalization peaked in August (34.7 %) and started in May and June.

The shortest term to get help out of a medical institution was on the first - the second day displayed by patients with salmonellosis (1.71 ± 0.05 on average), (p <0.05), the patients infected with various AEIs would usually come after 2 days of disease onset (2.11±0.18), (p <0.05). The latest terms were observed out of AEI-III Vir group – more than 2 days after disease onset (2.36±0.31) (p <0.05).

The most common is the gastroenteritis form (44.2 % - 81.8 %), (p <0.05). The second place among people sick with AEIs belongs to enterocolitis form (24.3 % - 27.7 %), (p <0.05). A separate mention is for AEI-III Vir - in this group every fifth patient has enteritis form (18.2 %), (p <0.05) beside gastroenteritis. In the third part of all salmonellosis patients were diagnosed with gastroenterocolitis (32.0 % - 44.2 %), (p <0.05). The rarest disease state was gastritis which absolutely absent in AEI-III vir and S-I S. typh groups (figure 2).
The most common factors at fault for infectious transition were milk products (22.6%), (p <0.05), vegetables and fruit (21.0%), (p <0.05), and for salmonella in particular – poultry eggs (40.8%), (p <0.05), meat and fish products (40.8%), (p <0.05), milk (36.8%), (p <0.05).

Based on indicators of clinical blood test of the observed groups during the periods of acute infection and early convalescence it was conducted the integrative indices of endogenous intoxication and their statistic-based analysis.

The white cell count in both AEI and salmonellosis was in the normal levels and it was not correlated with etiology of disease. For example, the AEI-all group (70 people) the average leukocyte count was (8.13 ± 0.36) x 10^9/l, in S-all (140 people) it was (7.86 ± 0.27) x 10^9/l, (p <0.05). The AEI-III Vir patients, however, had a drastically lower white cell count (p <0.05) in comparison to other sick.

The AEI-all group had in 5.1 times higher leukocyte intoxication index (LII) (4.06 ± 0.39) in comparison to normal (0.79 ± 0.10) (p <0.05): AEI-I - (4.30 ± 0.66), AEI-II Kl. - (3.41 ± 0.52), AEI-III - (4.53 ± 0.56), the correlation of these changes to separate causes weren’t observed, (p >0.05). Group S was labeled increased in 6.5 times higher (5.03 ± 0.36) in comparison with the norm, (p <0.05), S-I S. typh. - (4.61 ± 0.56), S-II S. ent. - (5.36 ± 0.46) and it was clearly not dependent on etiology of infection, (p >0.05). In comparison between AEI and S groups themselves, the index of S was 1.3 times bigger (p <0.05) (figure 3).

Hematological intoxication index (HII) in the surveyed groups increased in 6.5 times in total (5.10 ± 0.56) compared to the normal (0.79 ± 0.10), (p <0.05), in AEI-I - (5.55 ± 0.98), AEI-II Kl. - (3.95 ± 0.59), AEI-III Vir - (5.85 ± 0.52), (p <0.05). The group S has even seen further raise in 8.1 times - (6.41 ± 0.53) compared to norm (p <0.05), S-I S. typh. - (5.82 ± 0.88), S-II S. ent. - (6.83 ± 0.65), just like with LII there was no dependency on etiology of infection, (p >0.05). HII of salmonellosis patients in comparison with AEI was in 1.2 times bigger (p <0.05) (figure 3).

Leukocytes shift index (ISL) of AEI patients was increased in 2.4 times higher (4.35 ± 0.31) than normal (1.83 ± 0.10), (p <0.05): AEI-I - (4.70 ± 0.51), AEI-II Kl. - (4.00 ± 0.41), AEI-III Vir - (3.87 ± 0.54) , no correlation in between groups, (p >0.05). ISL of salmonellosis patients (4.25 ± 0.26) increased in 2.3 times, (p <0.05), in the absence of dependence on etiology S-I S. typh. - (4.23 ± 0.42), S-II S. ent. - (4.34 ± 0.33), (p >0.05). Any significant changes under comparison of AEI and salmonellosis using this coefficient were not observed (p >0.05) (figure 3).
All surveyed patients of AEI had ILymp decrease in 2.1 times lower (0.243 ± 0.018) compared to the norm (0.51 ± 0.030), (p < 0.05), in groups AEI-I - (0.240 ± 0.030), AEI-II Kl. - (0.250 ± 0.030), AEI-III Vir - (0.230 ± 0.020) there was no significant decrease in comparison on etiological sub-groups, (p >0.05). The records of patients with salmonella under survey showed that ILymp has decreased in 1.8 times compared to the norm (0.286 ± 0.018), (p <0.05), in S-I S. typh. - (0.259 ± 0.026), S-II S. ent. - (0.290 ± 0.022), no dependency to etiology of infection (p >0.05).

In the research of intestinal microbiocenosis at the period of acute infection it was discovered the following changes such as: the total count of bifidobacterium, lactobacillus and E.coli was in 2-3 lg lower than the comparison donors, and the count of all other OMO, hemolytic E.Coli and Candida fungi grew in 3 to 4 lg (p <0.05 - 0.001) (table 1).

### Table 1 - Dynamic shifts of intestinal microbiocenosis in cases of AEI and salmonellosis at the time of hospitalization (M±m)

<table>
<thead>
<tr>
<th>Group</th>
<th>Microorganisms (lg in Standard unit per g)/ % patients</th>
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<tbody>
<tr>
<td></td>
<td>Bifidoba-cteria</td>
</tr>
<tr>
<td>Comparison (n=20)</td>
<td>7.90±0.07/ 100</td>
</tr>
<tr>
<td>AEI-all (n=70)</td>
<td>5.44±0.25/ 100</td>
</tr>
<tr>
<td>AEI-I (n=37)</td>
<td>5.72±0.32/ 100</td>
</tr>
<tr>
<td>AEI-II Kl. (n=22)</td>
<td>4.85±0.54/ 100</td>
</tr>
<tr>
<td>AEI-III Vir (n=11)</td>
<td>5.20±0.55/ 100</td>
</tr>
<tr>
<td>S-all (n=140)</td>
<td>5.81±0.13/ 100</td>
</tr>
<tr>
<td>S-I S. typh. (n=43)</td>
<td>5.95±0.31/ 100</td>
</tr>
<tr>
<td>S-II S. ent. (n=97)</td>
<td>5.80±0.13/ 100</td>
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</tbody>
</table>

Note. Applicable difference of indicators (p<0.05-0.001): a –in regards to comparison group; b –AEI; c – salmonellosis ; d – in S sub-groups; e – in AEI sub-groups

The convalescents in S-all have shown a white cell count (7.95 ± 0.14) x 10^9/l that was higher if compared to AEI-all (p <0.05). After treatment of AEI-all group patients the white cell count was in 1.2 times lower (6.90 ± 0.33) x 10^9/l, (p <0.05). The lowest white cell count kept on the rate of group AEI-III Vir (5.73 ± 0.50), (p <0.05). There were no differences depending on etiology of infection in salmonellosis patients’ records observed.

After treatment the LII in AEI-all group has decreased in 3 times in comparison to time of hospitalization (1.37 ± 0.16), in groups AEI-I - (1.24 ± 0.23), AEI-II Kl. - (1.53 ± 0.24), AEI-III Vir - (1.41 ± 0.55), (p <0.05). The salmonellosis patients record (S-all) also shows a significant decrease in 3.9 times - (1.28 ± 0.08), in groups S-I S. typh. - (1.33 ± 0.13), S-II S. ent. - (1.24 ± 0.11), (p <0.05). There were no correlations depending on etiology of infection observed (figure 4).

HII in convalescent patients with acute enteric infections (AEI-all) has decreased in 3.2 times compared to hospitalization (1.60 ± 0.24), in groups AEI-I - (1.50 ± 0.38), AEI-II Kl. - (1.63 ± 0.25), AEI-III Vir - (1.85 ± 0.80), (p <0.05). In group S-all this index has decreased in 4.1 times (1.57 ± 0.11), in sub-groups S-I S. typh. - (1.60 ± 0.18) S-II S. ent. - (1.55 ± 0.14), (p <0.05) (figure 4).

ISL in cases of AEI compared to hospitalization was decreased in 2.3 times (1.88 ± 0.12), (p <0.05). The observed results prove that there was no correlation to etiology of infection: AEI-I - (1.95 ± 0.20), AEI-II Kl. - (1.80 ± 0.16), AEI-III Vir - (1.85 ± 0.26). In S-all convalescents this coefficient was in 1.9 times lower (2.25 ± 0.07) (p <0.05), and hasn’t been correlated to cause as well: observed in groups S-I S. typh. - (2.41 ± 0.14), S-II S. ent. - (2.18 ± 0.08). ISL of salmonella convalescents was higher than in AEI patients after treatment (p <0.05) (figure 4).
Survey of patients in group AEI-all has shown that $I_{\text{lymph}}$ has been normalized after treatment ($0.525 \pm 0.045$) and it was in 2.8 times higher than in S-all group ($0.186 \pm 0.018$), (p <0.05).

The analyses in period of convalescence and post-treatment have helped us to discover that those suffering with AEI had faster normalization of microflora than the convalescents with salmonellosis. Bifidobacteria and lactobacilli of AEI patients were significantly higher than in S-all groups, (p <0.05 - 0.001). There were still hemolytic organisms found in salmonella patients, but they were absolutely absent in AEI (p <0.05 – 0.001). Total count of OMO in feces in comparison to hospitalization period has been changed only in AEI-all, (p <0.05 – 0.001), the S group stayed the same. The Candida fungi total count has been normalized only in AEI patients’ microflora.

It should be noted the best indicators of microflora normalization in convalescent patients were observable in AEI-I and AEI-III Vir. groups (table 2).
Table 2 – Dynamic shifts of intestinal microbiocenosis of intestines in cases of AEI and salmonellosis after treatment (M±m)

<table>
<thead>
<tr>
<th>Group</th>
<th>Microorganisms (lg in Standard unit per g)/ % patients</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Bifidoba-cteria</td>
<td>Lactoba-cillus</td>
<td>E. coli total count</td>
<td>Hemolytic E. coli</td>
<td>Other OMO</td>
<td>Candida fungi</td>
<td></td>
</tr>
<tr>
<td>Comparison (n=20)</td>
<td>7,90±0,07/ 100</td>
<td>7,75±0,10/ 100</td>
<td>7,51±0,12/ 100</td>
<td>0,00±0,00</td>
<td>0,51±0,35/ 20,0</td>
<td>0,35±0,24/ 10,0</td>
<td></td>
</tr>
<tr>
<td>AEI all (n=70)</td>
<td>6,73±0,25/ 100</td>
<td>7,41±0,17/ 100</td>
<td>6,24±0,14/ 100</td>
<td>0,00±0,00</td>
<td>2,50±0,65/ 5,7</td>
<td>1,50±0,29/ 5,7</td>
<td></td>
</tr>
<tr>
<td>AEI-I (n=37)</td>
<td>6,92±0,29/ 100</td>
<td>7,58±0,13/ 100</td>
<td>6,54±0,18/ 100</td>
<td>0,00±0,00</td>
<td>1,50±0,50/ 5,4</td>
<td>1,50±0,50/ 5,4</td>
<td></td>
</tr>
<tr>
<td>AEI-II Kl. (n=22)</td>
<td>6,11±0,65/ 100</td>
<td>6,78±0,57/ 100</td>
<td>5,67±0,17/ 100</td>
<td>0,00±0,00</td>
<td>3,50±0,50/ 9,1</td>
<td>1,50±0,50/ 9,1</td>
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</tr>
<tr>
<td>AEI-III Vir (n=11)</td>
<td>7,00±0,41/ 100</td>
<td>7,75±0,25/ 100</td>
<td>5,75±0,25/ 100</td>
<td>0,00±0,00</td>
<td>0,00±0,00</td>
<td>0,00±0,00</td>
<td></td>
</tr>
<tr>
<td>S-all (n=140)</td>
<td>6,75±0,13/ 100</td>
<td>6,88±0,11/ 100</td>
<td>7,44±0,08/ 100</td>
<td>1,50±0,29/ 2,9</td>
<td>2,55±0,15/ 27,1</td>
<td>2,06±0,17/ 12,9</td>
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<tr>
<td>S-I. S. typh. (n=43)</td>
<td>6,68±0,25/ 100</td>
<td>6,84±0,24/ 100</td>
<td>7,42±0,14/ 100</td>
<td>1,50±0,50/ 4,7</td>
<td>2,82±0,33/ 25,6</td>
<td>2,50±0,29/ 9,3</td>
<td></td>
</tr>
<tr>
<td>S-II S. ent. (n=97)</td>
<td>6,75±0,14/ 100</td>
<td>6,87±0,11/ 100</td>
<td>7,45±0,10/ 100</td>
<td>1,50±0,50/ 2,1</td>
<td>2,41±0,15/ 27,8</td>
<td>1,93±0,20/ 15,5</td>
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</tbody>
</table>

Note. Applicable difference of indicators (p<0,05-0,001): a – for the comparison group; b – AEI; c – salmonellosis; r – in group S; e – in the period of acute infection; f – in group AEI;

CONCLUSIONS

1. In etiological statistics for AEI patients the prevailing causes are Klebsiella pneumoniae (31.4 %), viruses (15.7 %), E. coli (11.4 %), Pseudomonas aeruginosae (10.0 %), (p <0,01). Salmonellosis is caused by 2 dominant strains of the same disease S. enteritis (69.0 %), S. typhimurium (31.0 %), (p <0,01).

2. The research of integrative markers on intoxication allowed us to state the fact that endogenous intoxication rises up in any patient during the acute infection periods, but it’s rate is more affirmed in cases of salmonellosis and is connected to it’s cause (p <0,05 – 0,001).

3. The intoxication syndrome in its acute period can be perceived via integrative markers of endogenous intoxication, which are significantly higher in infected patients. HII in AEI-all increased in 5.1 times (p <0,05), in S-all – 6.5 times (p <0,05) and higher in comparison between disease groups – in 1.3 times. HII in AEI-all group increased in 6.5 times (p <0,05), and in S-all it was in 8.1 times higher (p <0,05) which in 1.2 times more than in AEI patients. ISL was increasing independently of etiology in all groups in 2.3 – 2.4 times higher (p <0,05). Ilymph was observably decreased as well in 1.8 – 2.1 times less (p <0,05).

4. The observations of intestinal microflora and microbiocenosis at acute period of infection show less count of bifidobacteria, lactobacilli and E.coli while an increase in other OMO, the hemolytic E.coli and Candida fungi can also be observed (p <0,05 – 0,001).

5. The microflora normalized faster in AEI convalescent patients in comparison to those who have suffered with salmonellosis. Levels of bifido- and lactobacteria in AEI convalescents were higher in comparison to S-all patients (p <0,05 – 0,001). Besides of that, S convalescents
were still having a big amount of hemolytic microorganisms. This tendency was absent in AEI patients who were absolutely clean of them (p<0.05 – 0.001). Level of other OMO in organism (p <0.05 – 0.001), the others had no changes. The tendency to normalization of Candida fungi count was observed only in AEI convalescents.

**Sorce of fund:** no

**Conflict of interest:** no

**Authors’s contribution:**

**Data gathering and idea owner of this study:**

Oksana Chemych, Mykola Chemych;

**Study design:** Oksana Chemych, Mykola Chemych, Oleh Berest;

**Data gathering:** Oksana Chemych, Oleh Berest, Nina Malys, Diana Svorydenko;

**Writing and submitting manuscript:** Oksana Chemych, Mykola Chemych, Oleh Berest, Oleksandr Suprun, Diana Svorydenko;

**Editing and approval of final draft:** Oksana Chemych, Mykola Chemych, Oleh Berest, Oleksandr Suprun, Nina Malys.

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