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Surveillance of Multi-drug resistance of *Salmonella Typhimurium* strains. Twenty years review.

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ABSTRACT

Today all over the world *Salmonella typhimurium* is one of the most frequent causes of food poisoning in humans. The antimicrobial resistance of salmonellas has increased rapidly during the last decade, creating a serious threat to the treatment of infectious diseases. This study will introduce the multi-drug resistance of 2931 *Salmonella typhimurium* strains isolated in patients diagnosed with salmonellosis or in carriers of salmonellas in the region of Elbasan, Albania during 1985-2004. All *Salmonella typhimurium* strains isolated during this period have been tested using impregnated discs with the most common used antimicrobial agents. *S.typhimurium* strains have shown resistance toward antibiotics as follows: Te+S, 64.04%, Te+C, 58.24%; S+C, 55.85%, Te+S+C, 53.46% while the multi-drug resistance shown is 87.17%. This multi-drug resistance of the strains isolated during 1985-2004 is comparable with the data represented by some native and international authors.

Keywords: antibiotics, double drug resistance, multi-drug resistance, *Salmonella typhimurium*.

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INTRODUCTION

Today all over the world *Salmonella typhimurium* is one of the most frequent causes of food poisoning in humans. Studying and analyzing the antimicrobial resistance of the *Salmonella typhimurium* strains is of a great importance and of great theoretical and practical value. Treating the infected patients with the right antibiotics is a necessity and strongly recommended. The early usage of antibiotics in medical practice has noted significant changes in treatment of infected people and carriers, eliminations of complications, prevention of epidemic outbreaks and decrease of salmonellosis cases. The first sulfanilamide resistant salmonellas were isolated after 1940s; the tetracyclines and chloramphenicol resistant strains were isolated in the '50s, ampicillin resistant strains during the '70s and during 1980s salmonellas showed resistance even against bactrim. During the last decade, they have shown resistance against very selected antibiotics causing a serious problem in the treatment of these effective diseases. The antimicrobial resistance of *Salmonella* strains is a very delicate issue for all public health authorities of all countries of the world, especially of the developing countries.^{4,5,8} This study will introduce and analyze the double-drug, triple-drug and multi-drug resistance of *Salmonella typhimurium* strains isolated in patients diagnosed with salmonellosis or in carriers of salmonellas in the region of Elbasan, Albania (no similar research has been conducted in this region before) during 1985-2004.

MATERIALS AND METHOD

2931 *Salmonella typhimurium* strains isolated in patients diagnosed with salmonellosis or in carriers of salmonellas in the region of Elbasan, have been examined. During these years, 228,740 individuals have been tested in day cares, kindergartens, schools etc. or some of them have been tested directly from National Microbiology Laboratory of Elbasan City (NMLEC). NMLEC registers have been used as the primary source of reference and we have worked in this institution during the years 1999-2004. All *S.typhimurium* strains isolated during this period have been tested using impregnated discs with these antimicrobial agents: Ampicillin (AM), Streptomycin (S), Tetracycline (TE), Chloramphenicol (C), Kanamycin (K), Gentamicin (GM), Bactrim (SXT), Nalidixic Acid (NA), Ciprofloxacin (CIP). The resistance of these strains will be determined based on the presence or absence of the growth inhibition zone around these agents.²

RESULTS AND DISCUSSION

2931 *Salmonella typhimurium* strains have been isolated in patients diagnosed with salmonellosis or in carriers of salmonellas in the region of Elbasan, Albania during 1985-2004.

The antimicrobial resistance of these isolated strains has been determined through the anitbiograms generated. As the most common antibiotics used daily in the treatment of patients and carriers of *Salmonella* are Tetracycline, Chloramphenicol and Streptomycin, the double and triple drug resistance against these antibiotics during 1985-1994 and 1995-2004 in Elbasan region has been analyzed. The annual numbers for each year and for all years in total are represented in the following tables.

Table 1. Frequency of *Salmonella typhimurium* strains isolated in Elbasan region during 1985-2004 which have shown double and triple drug resistance against antimicrobial agents (in percentage).

Years	No. of strains	Resistance			
		TE + S %	TE + C %	S + C %	TE + S + C %
1985	461	96.96	94.79	95.01	94.36
1986	411	84.67	83.94	84.42	83.21
1987	590	71.35	56.70	55.42	54.40
1988	688	38.20	38.22	29.50	25.58
1989	347	55.33	38.61	39.19	37.46
1990	114	17.54	14.03	21.05	15.78
1991	113	39.82	34.51	26.54	27.43
1992	71	53.52	63.38	52.11	49.29
1993	70	54.28	58.57	50.00	47.14
1994	15	86.66	80.00	86.66	80.00
1995	12	66.66	58.33	50.00	50.00
1996	11	54.54	63.63	72.72	27.27
1997	8	62.50	50.00	75.00	37.50
1998	27	70.37	62.96	50.00	66.66
1999	4	75.00	25.00	0.00	25.00
2000	4	50.00	25.00	25.00	25.00
2001	0	0.00	0.00	0.00	0.00
2002	4	75.00	25.00	25.00	25.00
2003	1	100.0	100.0	100.0	100.0
2004	0	0.00	0.00	0.00	0.00
1985-2004	2931	64.04	58.24	55.85	53.46

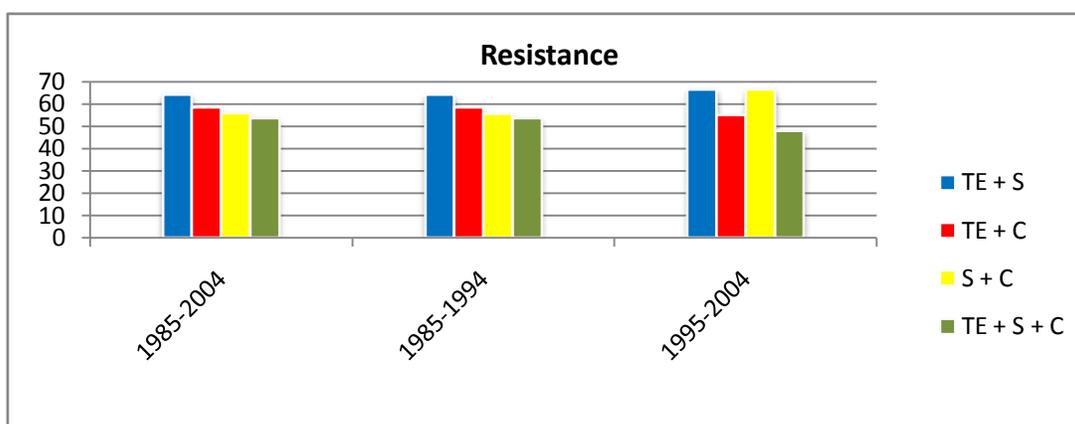
Table 1 shows that the double-drug resistance against Tetracycline - Streptomycin, (Te+S 64.04%) and Streptomycin-Chloramphenicol (S+C 55.85) has increased while the double-drug resistance against Tetracycline-Chloramphenicol (Te+C 58.24%) and triple-drug resistance against Tetracycline-Streptomycin-Chloramphenicol (Te+S+C 53.46%) has decreased over the course of years.

Table 2 presents the double and triple drug resistance against the antimicrobial agents during 1985-1994 and 1995-2004. This table shows that the double-drug resistance Te+S has been 63.99%; Te+C, 58.32%; S+C, 45.10%; and the triple-drug resistance Te+S+C has been 53.60%.

This shows that the antimicrobial resistance during 1985-1994 has been similar to the one shown during 1985-2004. During the second period 1995-2004 the double-drug resistance against Te+S has been 66.20%; Te+C, 54.93%; S+C, 66.20% and the triple-drug resistance against Te+S+C has been 47.89%. This is represented in Graph 1.

Table 2. Frequency of *Salmonella typhimurium* strains isolated in Elbasan region during 1985-1994 and 1995-2004 which have shown double and triple drug resistance against antimicrobial agents (in percentage).

Years	No. of Strains	Antimicrobial Resistance			
		TE + S %	TE + C %	S + C %	TE + S + C %
1985-1994	2860	63.99	58.32	55.59	53.60
1995-2004	71	66.20	54.93	66.20	47.89



Graph 1. Frequency of double and triple drug resistance of *Salmonella typhimurium* strains isolated in Elbasan region during 1985-2004 and during each time interval within this period (in percentage).

From this data, it can be concluded that the double-drug resistance against Tetracycline-Streptomycin and Streptomycin-Chloramphenicol has increased while the double-drug resistance against Tetracycline-Chloramphenicol and the triple-drug resistance against Tetracycline-Streptomycin-Chloramphenicol has decreased.

As *S.typhimurium* strains' resistance has increased all over the world and some of them have even shown a multi-drug antimicrobial resistance, the antimicrobial resistance of 2931 isolated *S.typhimurium* strains against 2-9 most common used antimicrobial agents (Ampicillin, Streptomycin, Tetracycline, Chloramphenicol, Kanamycin, Gentamicin, Bactrim, Nalidixic Acid, Ciprofloxacin) is analyzed in this paper.

The results are represented in Table 3.

Table 3. Frequency of multi-drug resistance of *Salmonella typhimurium* strains isolated in Elbasan region during 1985-2004 (in percentage)

Years	No. of strains	Resistance									
		Multiple-Drug Resistance									
		1	2	3	4	5	6	7	8	9	multiple
1985	461	0.00	1.30	0.43	4.77	20.39	25.16	41.65	3.69	-	97.83
1986	411	0.49	2.43	2.19	4.86	10.42	37.71	27.25	5.11	-	89.78
1987	590	0.34	3.05	15.25	10.85	2.20	17.12	27.12	16.44	-	81.02
1988	668	0.90	44.61	9.13	7.93	0.90	15.42	3.14	4.79	-	85.93
1989	347	1.44	10.95	21.32	5.19	6.05	11.24	13.83	6.05	-	74.64
1990	114	1.75	8.77	22.81	15.79	17.54	18.42	7.89	5.26	-	96.50
1991	113	0.00	7.08	22.12	15.04	16.81	17.70	7.08	5.31	-	91.15
1992	71	2.82	7.04	19.72	14.08	11.27	22.53	12.68	4.22	-	91.55
1993	70	2.86	17.14	20.00	18.57	12.86	14.28	11.43	2.86	-	97.14
1994	15	0.00	6.67	20.00	13.33	0.00	6.67	6.67	20.00	-	73.33
1995	12	0.00	0.00	25.00	8.33	16.67	8.33	25.00	0.00	-	83.33
1996	11	0.00	0.00	9.09	27.27	18.18	27.27	18.18	0.00	9.09	100.0
1997	8	0.00	12.50	12.50	12.50	25.00	12.50	12.50	12.50	0.00	100.0
1998	27	3.70	0.00	0.00	3.70	14.81	33.33	22.22	11.11	7.41	96.30
1999	4	0.00	0.00	0.00	0.00	25.00	50.00	0.00	75.00	0.00	100.0
2000	4	0.00	0.00	0.00	25.00	25.00	25.00	25.00	25.00	0.00	100.0
2001	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2002	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2003	4	25.0	0.00	25.00	0.00	25.00	0.00	0.00	0.00	25.0	75.00
2004	1	0.00	0.00	0.00	100.0	0.00	0.00	0.00	0.00	0.00	100.0
1985-2004	2931	0.78	13.89	11.05	8.36	8.36	20.44	19.82	7.40	0.14	87.17

Note: Sign (-) indicates that the antibiotic has not been applied.

Table 3 shows that the multi-drug antimicrobial resistance of the *Salmonella typhimurium* strains isolated in Elbasan region during 1985-2004 has fluctuated and 87.17% of the strains isolated during this period have shown multi-drug antimicrobial resistance.

Table 4. Frequency of multi-drug resistance of *Salmonella typhimurium* strains isolated in Elbasan region during 1985-1994 and 1995-2004 (in percentage)

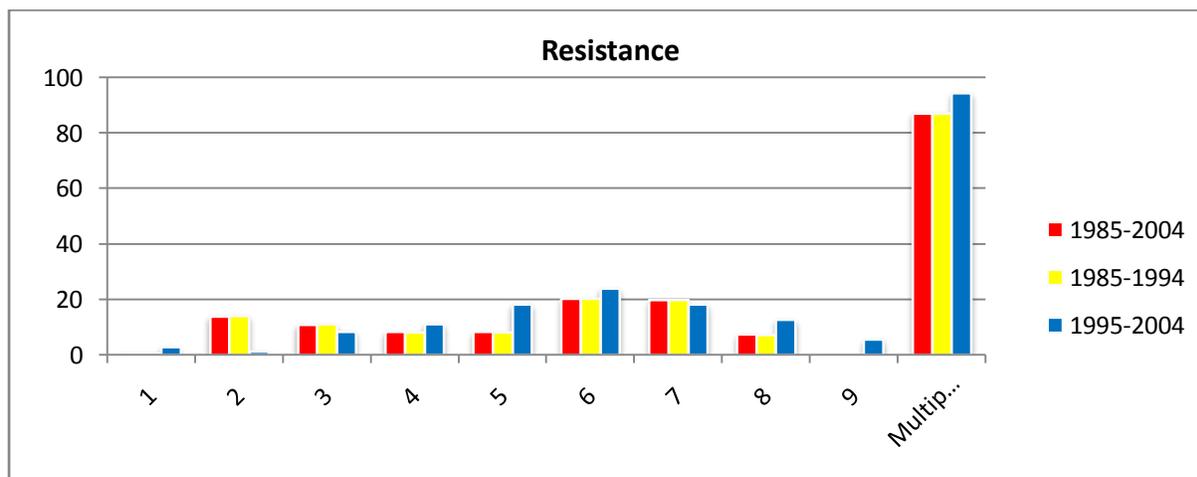
Years	No. of Strains	Antimicrobial Resistance									
		Multiple-Drug Resistance									
		1	2	3	4	5	6	7	8	9	Multip
1985-1994	2860	0.73	14.20	11.12	8.29	8.11	20.35	19.86	7.27	-	86.99
1995-2004	71	2.81	1.41	8.45	11.27	18.31	23.94	18.31	12.68	5.63	94.37

Note: Sign (-) indicates that the antibiotic has not been applied

Table 4 shows that the multi-drug antimicrobial resistance of the *Salmonella typhimurium* strains isolated in Elbasan region during 1985-1994 has fluctuated and 86.99% of the strains isolated

during this period have shown multi-drug antimicrobial resistance and this is very close to the resistance shown during the twenty years period.

It is concluded from Table 4 that 94.37% of *S.typhimurium* strains isolated in Elbasan region from 1995-2004 have shown multi-drug antimicrobial resistance against 2-9 antimicrobial agents used. The multi-drug antimicrobial resistance of the *S.typhimurium* strains isolated during this time has increased and this is represented in Graph 2.



Graph 2. Frequency of multi-drug resistance of *Salmonella typhimurium* strains isolated in Elbasan region during 1985-2004, 1985-1994 and 1995-2004 (in percentage).

Analyzing the data displayed on the tables and graphs in this paper, it is obvious that *Salmonella typhimurium* strains have shown high resistance against antimicrobial agents like Streptomycin, Tetracycline and Chloramphenicol and against multiple combinations of these antimicrobial agents.

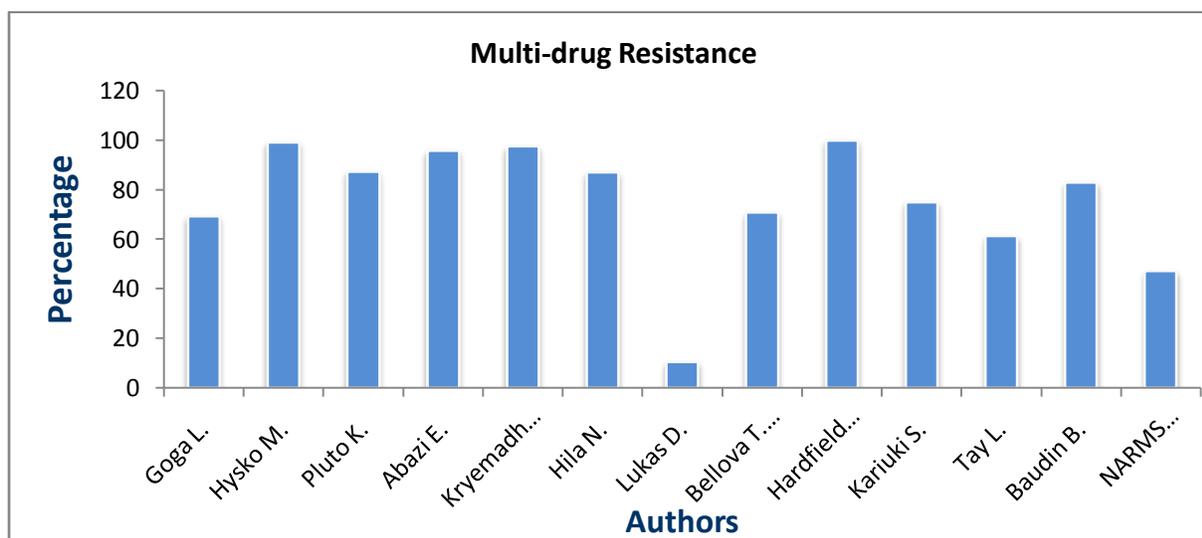
This may be due to application of the antimicrobial agent against these strains without performing the antibiograms first or a lot often the medical practitioners have prescribed and used these antimicrobials agents intensively for the treatment of salmonellosis. This has lowered the sensitivity of the bacteria and has increased the antimicrobial resistance against these antimicrobial agents.

Another explanation can be that the carriers usually get over the counter medication without being consulted first with a physician who may prescribe a combination of such antimicrobial agents. This multi-drug resistance trend of the strains isolated during 1985-2004 in Elbasan region is comparable with the data represented by some native and international authors and this is represented in Table 5.

Table 5. Multi-drug resistance of *Salmonella typhimurium* strains isolated in our country, Albania and in other countries.

Author	Place	Year	Multi-drug resistance
Goga L.	Fier	1983	69.23
Hysko M.	Tirane	1990	99.17
Puto K.	Gjirokaster	1995	87.4
Abazi E.	Fier	2001	95.87
Kryemadhi A.	Durres	2001	97.51
Hila N.	Elbasan	2004	87.17
Lukas D.	Kroatia	2000	10.46
Bellova T.N.	Russia	1982	70.8
Hardfield T.C.	Liberia	1982	100.0
Kariuki S.	Kenya	1996	75.00
Tay L.	Singapor	1992	61.3
Baudin B.A.	Canada	2001	83.0
NARMS 2000	Sh.B.A.	2000	47.2

The multi-drug resistance of the *S.typhimurium* strains during 1985-2004 and during 1985-1994 has been respectively 87.17% and 86.99%, which is close with the resistance met in Gjirokaster, 1995 (14); Canada, 2001 (6); while this resistance has jumped to 94.37% during 1995-2004 which is close to the resistance met in Fier, 2001 (1); Durres, 2001 (10) and these percentages differ from what has been reported by other authors as per Table 5 and Graph 3.



Graph 3. Multi-drug resistance of *Salmonella typhimurium* strains isolated in our country and in some other countries of world (in percentage).

CONCLUSION

Salmonella typhimurium strains isolated during 1985-2004 have shown double-drug resistance against antimicrobial agents as follows: Te+S, 64.04%; Te+C, 58.24%; S+C, 55.85% and triple-drug antimicrobial resistance against Te+S+C has been 53.46%. The double and triple drug-

resistance observed during 1985-1994 was Te+S, 63.99; Te+C, 58.32%; S+C, 45.10% and Te+S+C was 53.60%. It was observed that during 1995-2004, the double-drug resistance against Tetracycline + Streptomycin, Tetracycline + Chloramphenicol, and Streptomycin + Chloramphenicol is increased in comparison with the other period of this study. The average percentages of this antimicrobial resistance shown has been Te+S, 66.20%; Te+C, 54.93%, S+C, 66.20% and the triple-drug resistance Te+S+C has been 47.89%. The multi-drug resistance of these strains has been 87.17%. *Salmonella typhimurium* strains have shown double, triple and multi drug resistance against 2-9 antimicrobial agents. This is mainly due to the application of these agents without performing the antibiograms initially.

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