Testing parameters used in risk quantification of enteric infections

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RESUMEN

Las infecciones entéricas implican una inmensa carga incluyendo incapacidad, desarrollo deficiente y muerte del huésped. La Organización Mundial de la Salud en 2013 estimo 760,000 muertes en niños menores de 5 años principalmente en el 3er mundo. La evaluación de riesgo de infección permite predicciones que informan a la política ambiental, investigación y aplicación de recursos para prevenir y atacar infecciones. Aquí se trata de evaluar o probar el grado de dependencia de parámetros en las funciones de evaluación de riesgo de infección, mediante la asociación estadística. Los parámetros y variables observados fueron: la concentración en biosólidos, decaimiento en el ambiente, respuesta a dosis, expresión, y dimensión o tamaño del patógeno. Se encontraron correlaciones estadísticamente significativas entre casos de hospitalizaciones y concentración de gérmenes en biosólidos Clase B y en excreciones. Estos hallazgos sirven de prueba de validación tanto de las ecuaciones como de los parámetros de los modelos de cálculo de riesgo de infección. No se encontraron asociaciones contradictorias.

Palabras clave: infecciones entéricas, diarrea niños, parámetros patogénicos.

ABSTRACT

The global burden meant by enteric infections includes incapacities, poorly developed children, ill nutrient absorption, and death of the host; indeed in the year 2013 the World Health Organization reported 760,000 deaths per year in children fewer than 5 years old, mainly in developing countries. The risk quantification of infections informs environmental policy, and research to prevent and to control diseases. This work intends to introduce a simple test for the parameters effect in the risk quantification models, by analyzing the associations between hospitalized cases and: germs concentration in biosolids, decay, dose-response, shedding, and diameter or length of the pathogen. The strong associations found here between hospitalized cases and concentration of germs, in biosolids Class B and concentration in shed masses, between decay rate and dose response parameters, and between decay rate and biosolids concentration, serve as validation test of models and parameters of risk of enteric infection calculations. Interesting to notice that association between cases and concentration of germs in shedding is higher than concentration in biosolids. Here were found not contradictory associations.

Key words: children diarrhea, enteric infections, pathogenic parameters.

INTRODUCTION

The burden of enteric infections mean about 2.2 million deaths globally and 760,000 diarrhea-deaths in children less than 5 years old. The World Health Organization (WHO), found rotavirus as the highest cause of diarrhea in children in 2009 (WHO, 2009), for which the use of a rotavirus vaccine will prevent severe diarrhea and dehydration among children, helping to reduce the number of deaths, however the incidence of enteric infections keeps almost as large as before (Petri *et al*., 2008, WHO, 2013). The common sources of infection are: contaminated food or water, and passing of shed germs (human, livestock). This work examined associations among hospitalized cases due to enteric infections and some parameters and variables included in the models of risk of infection. Developing countries are more strongly affected by infections of all kinds, in these countries about 1.1 billion people have no safe drinking water and 2.6 billion lack of appropriate disposal of excretions (pit latrines) (Petri *et al*., 2008, Viau *et al*., 2011,WHO 2013)

In this work, we try to learn from the associations between cases actually hospitalized by enteric infection by each pathogen revised, and convenient variables. The pathogens observed here were: *E.coli* 0157*, Shigella, Campylobacter, Salmonella no typhi*, and Norovirus; the parameters and variables: decay rate, dose response, initial concentration in Class B biosolids, concentration in excretion of livestock animals, and size of the germs.

METHODS

The calculation of bivariate correlation coefficients between hospitalized cases, and selected parameter or variable, is supposed to evaluate their associations and therefore their goodness in calculating risk of infection, if the dependences between risk and parameter are modeled by monotonically changing functions. When an independent variable grows in a monotonically growing function, the dependent variable will necessarily grow, therefore if let's say the parameter "k" grows it is expected that the risk of infection will grow as well.

The risk calculations are based upon known functions, here considered the exponential dose-response function which is a monotonically growing function of both: ingested dose variable, and of dose-response parameter "k", this function is increasing in proportion to concentrations of pathogens (biosolids and shedding). In other hand the risk is decreasing with the decay rate in the environment. The dependence of risk with size is more indirect. The dependence with size is not calculated by one equation and is not monotonically changing since size plays a role in the germ transport and fate in the environment as well as in the hosts, here we only will look for the statistical associations of size with final risk calculation, to learn from there.

Summarizing the dependence expected, perhaps coincidental to associations with risk of infection are:

1. Response parameter: monotonically growing relationship with risk implies "+" coefficient sign.
2. Decay rate in environment: monotonically decreasing relationship: "-" sign.
3. Concentration of pathogen in biosolids: growing, "+"
4. Concentration in shedding mass: growing, "+"
5. Radius, diameter or length of pathogen: not a single behavior, both: "+" or "-"

The variables correlated were: hospitalized cases (counts) by infection per each pathogen, maximum shedding in log units (amount of pathogens per gram e.g. Plaque Forming Units PFU/g), time lasting shedding (months) multiplied by mean shedding pathogens (PFU*months/g), concentration in biosolids Class B (colony forming units CFU/g, Plaque Forming Units PFU/g, oocyst/g, etc.), decay in the

environment, germs radius (cm) and response parameter “k”. The pathogens studied were: *E.coli* 0157, *Cryptosporidium sp, Shigella, Campylobacter, Salmonella no typhi,* and Norovirus.

The Centers of Disease Control and Prevention (CDC, 2013) published the annual incidence, hospitalization, and death of cases of infection per pathogen. The response and decay rate were searched in the literature as well as shedding rates, times and concentrations both in human and livestock and wild animal, however we could not find enough data for human shedding of enteric pathogens by the end of this project, therefore included shedding rates from cattle and livestock animals.

The statistical analyses and graphs were made with SPSS, 2007, v 16.0.

RESULTS AND DISCUSSION

The correlation significant at the 0.01 and 0.05 level (2-tailed) were found between: hospitalizations (cases) and concentration in biosolids (Pearson’s R=1, $p<0.001$ N=6), cases and shedding (maximum counts shed in log units) R=0.90, $p<.05$, N=5, concentration in biosolids with decay (R= - 0.928, $p<1$, N=6) and with response parameter (R=1, $p<0$, N=6), and between biosolids concentration and response (R=1, $p<0.001$, N=6) see Table 1, listing Spearman’s non parametric correlation coefficients.

The Pearson’s correlation is significant for hospital and biosolids concentration (R= 1, $p<0.0001$, n=6), but not significant for hospital and shedding. Inversely the correlation between hospital and shedding is significant in Spearman’s coefficient calculation. The reminded significant correlations were significant in both algorithms Pearson’s and Spearman’s. Since Spearman’s are not parametric correlations, are not assumed Gaussian distribution of populations. Here present only the Spearman’s because these do not assume Gaussian distribution of populations.

The size of the germs is negatively and significantly correlated to shedding mass (maximum shedding mass: Pearson’s R=-1, n=2) and negatively but weakly associated to cases, and decay, but there are only three data points, therefore there is no power to conclude.

***Table 1**. Spearman's correlation coefficients indicating that maximum shedding rates are strongly associated with hospitalized cases*

		hospital	shed x time	Max shedd	Conc Biosol	Decay Mean	radius	response Mean
hospital	Coeff	1.000	.600	.900*	.464	-.486	-.866	.464
	Sig.	.	.208	.037	.354	.329	.333	.354
	N	6	6	5	6	6	3	6
shedxTim	Coeff	.600	1.000	.800	-.058	.143	-.866	-.058
	Sig.	.208	.	.104	.913	0.79	.333	.913
	N	6	6	5	6	6	3	6
Maxshedlog zNh	Coeff	.900*	.800	1.000	.359	-.400	-1.00	.359
	Sig.	.037	.104	.	.553	.505	.	.553
	N	5	5	5	5	5	2	5
Conc_sep	Coeff	.464	-.058	.359	1.000	-.928**	.000	1.000**
	Sig.	.354	.913	.553	.	.008	1.000	.
	N	6	6	5	6	6	3	6
decaymeanJT	Coeff	-.486	.143	-.400	-.928**	1.000	-.866	-.928**
	Sig.	.329	.787	.505	.008	.	.333	.008
	N	6	6	5	6	6	3	6
radius	Coeff	-.866	-.866	-1.000**	.000	-.866	1.000	.000
	Sig.	.333	.333	.	1.000	.333	.	1.000
	N	3	3	2	3	3	3	3
respMean	Coeff	.464	-.058	.359	1.000**	-.9276**	.000	1.000
	Sig.	.354	.913	.553	.	.008	1.000	.
	N	6	6	5	6	6	3	6

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

CONCLUSIONS

The strong associations between hospitalized cases and concentration of germs, in biosolids Class B and concentration in shed masses, are as expected, supporting the functional proportionality between risk of infection and concentration (ingested). The shedding data used is for livestock animals, which miss the human-host self-infection factor, as well as transmission to household companions.

The high significance in the negative associations between decay and response parameters existed in both, Pearson's and Spearman's algorithms, as theoretically expected.

Therefore from these associations the functional relationship of decay rate, dose response, and dose concentration, in the mathematical models for risk calculations are validated. The validation serves for the parameters used as well as for the equations constituting the models of risk of enteric infection. In addition, the shedding of germs in cattle and livestock seem strongly associated to risk of enteric infections.

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