DIETARY EXPOSURE ASSESSMENT OF TETRACYCLINE RESIDUES IN CHICKEN MEAT ON CHILDREN AND ADULTS IN PENINSULAR MALAYSIA

MARZURA, M. R.[1], MAHYUDIN, N. A.[2,3*], SYARIENA, A.[3], CHAI, L. C.[4], UNGKU FATIMAH, U. Z. A[2], MARNI, S.[5] AND KHAIRUNNISAK, M.[6]

1 Makmal Kesihatan Awam Veterinar, Bandar Baru Salak Tinggi, 43900 Sepang, Selangor
2 Faculty of Food Science and Technology, Universiti Putra Malaysia (UPM), 43400 UPM, Serdang, Selangor
3 Halal Products Research Institute, Universiti Putra Malaysia (UPM), 43400 UPM, Serdang, Selangor
4 Faculty of Science, University of Malaya, 50603 Kuala Lumpur
5 Veterinary Research Division, Department of Veterinary Services, Wisma Tani, 62624 Putrajaya
6 Southern Zone Veterinary Laboratory, 80350 Johor Bahru, Johor
**Corresponding author*: norainy@upm.edu.my

ABSTRACT. An exposure assessment was conducted to quantitate tetracyclines (TCs) in chickens and the risk estimates were calculated using deterministic and probabilistic approaches. The results revealed that through deterministic approach, estimated daily exposure to TCs resulted in children aged 1<y<3 and 4<y<6 (0.05919 and 0.03946 µg/kg bw/day), followed by adults (0.02847 µg/kg bw/day) and children aged 7<y<10 at 0.02631 µg/kg bw/day. Based on the probabilistic approach, dietary exposure of Malaysian adults to TCs was estimated to range from 0.00174–0.35209 µg/kg bw/day. In comparison, for the children group, the estimated exposure was higher in age 1<y<3 at 0.0137 – 1.9845 µg/kg bw/day followed by children aged 4<y<6 and 7<y<10 at 0.00718 – 1.3967 µg/kg bw/day and 0.00834 – 0.91841 µg/kg bw/day respectively. However, the estimated risk calculated for all groups was <10 % ADI. These indicate that toxicological risk with regard to the consumption of chicken meat could not be considered as a public health problem, but the result can be supportive for the safety authorities to engage policies in managing any potential risk. The occurrence of high concentration of TCs residues in small samples still warrants closer monitoring and management of the use of TCs in chicken farms in Peninsular Malaysia.

Keywords: chicken meat, dietary exposure assessment, deterministic, probabilistic, estimated risk

INTRODUCTION

Poultry products such as meat and eggs are important protein sources to humans. The use of veterinary drugs is range management, which the mode of drugs administered is either in the feed or drinking water. Among those drugs applied in veterinary medicine, tetracycline is routinely used due to its function which can react against many types of gram-negative and gram-positive bacteria in various food-producing animals, including cattle, sheep, pig and poultry (Vragović *et al.,* 2012). Tetracyclines (TCs) have been extensively used in animal husbandry practices; with oxytetracycline (OTC), tetracycline (TTC), chlortetracycline (CTC) and doxycycline (DC) being the four most common. The TCs are widely used to prevent and treat diseases due to bacterial infections and serve as growth promoters in poultry (Aalipour *et al.,* 2015; Salama *et al.,* 2011). Improper use of antibiotics has resulted in residues of drugs in animal products (Gonzalez Ronquillo & Angeles Hernandez, 2017). Subjected to the amount of residue present, such residues may constitute important health risk to consumer and initiate public health concerns. Therefore, antibiotics' safety and appropriate use remain among the most challenging public health issues and have become a global concern *(Darko et al.,* 2015; Salama *et al.,* 2011; Vutey *et al.,* 2012). Moreover, exposure to low-level doses of the antibiotic residues in foodstuffs may lead to the development of resistant strains of human pathogenic bacteria which can potentially cause allergic reactions in hypersensitive individuals (Cetinkaya *et al.,* 2012; Darko *et al.,* 2015; Vragović *et al.,* 2012)

In Malaysia, The Department of Veterinary Services (DVS) under the Ministry of Agriculture is the regulatory body that controls and monitors the presence of antibiotic residues in food of animal origins. The tolerance level or maximum residue limits (MRLs) established for four widely used TCs are 100 μg/kg for TC, OTC and/or CTC (parent drug, singly or in combination) and 100 μg/kg for DC in all food-producing animal (Food Act 1983 (Act 281) and Food Regulations 1985, 2015). Because of the aforementioned, the need to monitor for the presence of veterinary drug residues in food of animal origins such as poultry meat is a must (Croubels *et al.,* 2004). Therefore, as a first step towards assessing potential health risks to the consumers posed by TCs residues in Malaysian poultry, this study is conducted to evaluate the level of intake (exposure) of TCs residues in chicken meat among adults and children in Peninsular Malaysia.

The residue levels of TCs have been reported by Marzura *et al*. (2018) and the results were further utilized to assess public health risks associated with antibiotic residues through consumption of chicken in Peninsular Malaysia. An exposure assessment was conducted to detect and quantitate tetracycline, sulfonamide and quinolones. The results were then applied to calculate the risk estimates using deterministic and probabilistic approaches.

MATERIALS AND METHODS

Drug Residue Data

The occurrence of veterinary drug residues in 637 chicken meat samples originating from 320 small and medium scale chicken slaughterhouses in Peninsular Malaysia was presented in detail in our previously published work (Marzura *et al.,* 2018). The presence of TC residues was confirmed in 10 (1.6 %) samples while 6 (0.9 %) of these samples contained oxytetracycline (OTC) and doxycycline (DC) that were detected at concentrations above the established MRLs.

Food Consumption Data

Children Food Consumption Data

Malaysian Dietary Guidelines for Children and Adolescents 2013 recommended 14 g protein per serving, equivalent to one piece of chicken drumstick for children aged 7–12 years old. However, children aged 3–6 years old need only half piece of chicken drumstick per serving. The quantity of recommended serving is based on daily caloric needs by age group (Committee & Ministry, 2013).

Adult Food Consumption Data

The chicken meat consumption data for adults are gathered from the Malaysian Adult Nutritional Survey (MANS). The cross-sectional population survey covered all states in Peninsular Malaysia, including Sabah and Sarawak in East Malaysia, involving up to 4,000 representatives of Malaysian adults aged between 18 to 59 years old. A quantitative food frequency questionnaire (FFQ) was used. The selected participants were interviewed in their homes, workplaces, and any other comfortable and convenient vicinity. None of the respondents were not pregnant or breastfeeding at the time of the interview and not on any specific diet due to illness. Therefore, the chicken consumption data were based on eater-only data (Institute for Public Health (IPH), 2014).

Dietary Exposure Assessment

Dietary exposure assessment was conducted using deterministic (point estimate) and probabilistic (distribution-based or population-related) approaches targeting two groups: children and adults. Chicken meat consumption data for the adult population were obtained at 99th percentile and used in the deterministic exposure assessment. However, for children consumption, the data were taken within five times recommended serving as 14 g per serving of chicken drumstick. Whereas for probabilistic determination, for adults – the lowest (10th percentile), the highest (95th percentile) and average intake (mean) were used. For children, the value taken was ½ serving (7 g), recommended serving size (14 g) and three times serving (42 g). All data were computed in @Risk software™. The risk associated with the TCs residue through chicken meat consumption was calculated using the following equations:

$$Dietary\ exposure\ \frac{(\mu g}{kg\ bw/day)} = \frac{\Sigma\ [(Residue\ concentration\ \frac{(\mu g}{kg)} \times Food\ consumption\ (\frac{g}{day})]}{Body\ weight\ (kg)}$$

$$\%\ ADI = \frac{100 \times Dietary\ exposure\left(\frac{\mu g}{kg\ bw/day}\right)}{\left(\frac{\mu g}{kg\ bw/day}\right)}$$

RESULTS

Deterministic Analysis of the Dietary Tetracycline Exposure Assessment

Table 1. shows that the estimated dietary intake (EDI) of tetracycline ranged from 0.00921 µg/kg bw/day (adult) to the maximum of 0.05919 µg/kg bw/day (children 1 < y < 3), with the acceptable daily intake (ADI) of 0.03 % and 0.2 %, respectively. By looking at the results comparing men and women, men (0.01466 µg/kg bw/day to 0.02847 µg/kg bw/day) showed slightly higher exposure compared to women (0.01221 µg/kg bw/day to 0.02372 µg/kg bw/day), approximately about 0.002 µg/kg bw/day to 0.005 µg/kg bw/day differences. Consumers in urban area (0.01435 µg/kg bw/day to 0.02787 µg/kg bw/day) were more exposed to tetracycline compared to rural area (0.01227 µg/kg bw/day to 0.02383 µg/kg bw/day) as the consumption of the chicken meat is high in urban adult population compared to rural area. Among different ethnics, Chinese (0.01318 µg/kg bw/day to 0.02559 µg/kg bw/day) were found to be exposed to tetracycline residue through chicken meat consumption which is slightly higher compared to Malay (0.01311 µg/kg bw/day to 0.02546 µg/kg bw/day). Intakes in Chinese and Malay were higher compared to Indian (0.00921 µg/kg bw/day to 0.01788 µg/kg bw/day) at approximately 1.4 times. Generally, the estimated dietary intake of tetracycline for the Peninsular Malaysia adult population through chicken meat consumption is 0.01323 µg/kg bw/day to 0.02569 µg/kg bw/day to 0.04 % to 0.09 % of the defined ADI.

Table 1. Estimated dietary intake (µg/kg bw/day) to tetracycline residues[a] in children and adult from deterministic analysis: Lower to higher bound scenarios.

Categories			Deterministic					
			Lower bound scenario		Medium bound scenario		Higher bound scenario	
			EDI (µg/kg bw/day)[b]	%ADI[c]	EDI (µg/kg bw/day)	%ADI	EDI (µg/kg bw/day)	%ADI
Children	1<y<3		0.01612	0.05	0.03048	0.10	0.05919	0.20
	4<y<6		0.01075	0.04	0.02032	0.07	0.03946	0.13
	7<y<10		0.00717	0.02	0.01355	0.05	0.02631	0.09
Adults	Peninsular Malaysia		0.00700	0.02	0.01323	0.04	0.02569	0.09
	Gender	Men	0.00776	0.03	0.01466	0.05	0.02847	0.09
		Women	0.00646	0.02	0.01221	0.04	0.02372	0.08
	Strata	Urban	0.00759	0.03	0.01435	0.05	0.02787	0.09
		Rural	0.00649	0.02	0.01227	0.04	0.02383	0.08
	Ethnic	Malay	0.00694	0.02	0.01311	0.04	0.02546	0.08
		Chinese	0.00697	0.02	0.01318	0.04	0.02559	0.09
		Indian	0.00487	0.02	0.00921	0.03	0.01788	0.06

[a]Mean residue concentration in the chicken meat sample as follow: LB: 27.64 µg/kg, MB: 52.25 µg/kg and HB: 101.47 µg/kg
[b]Estimated Daily Intake (EDI): [(Chicken consumption X residue concentration /1000)/body weight] X correction factor
[c]Average Daily Intake (%): (EDI X 100)/30 µg/kg (ADI for tetracycline)

Table 2. Probabilistic analysis results of estimated tetracycline intake (µg/kg bw/day): Lower bound scenario.

Parameter		Mean	% ADI	SD	P50	% ADI	P90	% ADI	P95	% ADI
Children	(1<y<3)	0.09456	0.32	0.08000	0.07049	0.23	0.19953	0.67	0.25462	0.85
	(4<y<6)	0.06314	0.21	0.05360	0.04649	0.15	0.13377	0.45	0.17296	0.58
	(7<y<10)	0.04231	0.14	0.03625	0.03105	0.10	0.08983	0.30	0.11654	0.39
Adults	Peninsular Malaysia	0.02671	0.09	0.01823	0.02172	0.07	0.05235	0.17	0.06303	0.21
Gender (Adult)	Men	0.02963	0.10	0.02031	0.02390	0.08	0.05812	0.19	0.07014	0.23
	Women	0.02472	0.08	0.01702	0.01998	0.07	0.04840	0.16	0.05906	0.20
Strata (Adult)	Urban	0.02902	0.10	0.01986	0.02371	0.08	0.05709	0.19	0.06918	0.23
	Rural	0.02476	0.08	0.01691	0.02016	0.07	0.04813	0.16	0.05894	0.20
Ethnicity (Adult)	Malay	0.02648	0.09	0.01808	0.02145	0.07	0.05178	0.17	0.06247	0.21
	Chinese	0.02662	0.09	0.01820	0.02164	0.07	0.05208	0.17	0.06292	0.21
	Indian	0.01858	0.06	0.01286	0.01514	0.05	0.03639	0.12	0.04488	0.15

Note: SD = Standard deviation; P50 = at 50th percentile; P90 = at 90th percentile; P95 = at 95th percentile

Table 3. Probabilistic analysis results of estimated tetracycline intake (µg/kg bw/day): Medium bound scenario.

Parameter		Mean	% ADI	SD	P50	% ADI	P90	% ADI	P95	% ADI
Children	(1<y<3)	0.10941	0.36	0.08638	0.08480	0.28	0.22300	0.74	0.28262	0.94
	(4<y<6)	0.07324	0.24	0.05756	0.05650	0.19	0.14985	0.50	0.19089	0.64
	(7<y<10)	0.04874	0.16	0.03850	0.03749	0.12	0.10105	0.34	0.12857	0.43
Adults	Peninsular Malaysia	0.03101	0.10	0.01936	0.02613	0.09	0.05816	0.19	0.06923	0.23
Gender (Adult)	Men	0.03430	0.11	0.02120	0.02932	0.10	0.06397	0.21	0.07601	0.25
	Women	0.02860	0.10	0.01784	0.02413	0.08	0.05385	0.18	0.06399	0.21
Strata (Adult)	Urban	0.03362	0.11	0.02104	0.02839	0.09	0.06283	0.21	0.07548	0.25
	Rural	0.02876	0.10	0.01792	0.02441	0.08	0.05377	0.18	0.06433	0.21
Ethnicity (Adult)	Malay	0.03071	0.10	0.01911	0.02596	0.09	0.05761	0.19	0.06831	0.23
	Chinese	0.03089	0.10	0.01932	0.02611	0.09	0.05822	0.19	0.06891	0.23
	Indian	0.02161	0.07	0.01381	0.01819	0.06	0.04091	0.14	0.04876	0.16

Note: SD = Standard deviation; P50 = at 50^{th} percentile; P90 = at 90^{th} percentile; P95 = at 95^{th} percentile

Table 4. Probabilistic analysis results of estimated tetracycline intake (µg/kg bw/day): Higher bound scenario.

Parameter		Mean	% ADI	SD	P50	% ADI	P90	% ADI	P95	% ADI
Children	(1<y<3)	0.10941	0.36	0.08638	0.0848	0.28	0.2230	0.74	0.28262	0.94
	(4<y<6)	0.07324	0.24	0.05756	0.0565	0.19	0.1499	0.50	0.19089	0.64
	(7<y<10)	0.04874	0.16	0.03850	0.03749	0.12	0.1011	0.34	0.12857	0.43
Adults	Peninsular Malaysia	0.03101	0.10	0.01936	0.02613	0.09	0.0582	0.19	0.06923	0.23
Gender (Adult)	Men	0.0343	0.11	0.02120	0.02932	0.10	0.0640	0.21	0.07601	0.25
	Women	0.0286	0.10	0.01784	0.02413	0.08	0.0539	0.18	0.06399	0.21
Strata (Adult)	Urban	0.03362	0.11	0.02104	0.02839	0.09	0.0628	0.21	0.07548	0.25
	Rural	0.02876	0.10	0.01792	0.02441	0.08	0.0538	0.18	0.06433	0.21
Ethnicity (Adult)	Malay	0.03071	0.10	0.01911	0.02596	0.09	0.0576	0.19	0.06831	0.23
	Chinese	0.03089	0.10	0.01932	0.02611	0.09	0.0582	0.19	0.06891	0.23
	Indian	0.02161	0.07	0.01381	0.01819	0.06	0.0409	0.14	0.04876	0.16

Note: SD = Standard deviation; P50 = at 50^{th} percentile; P90 = at 90^{th} percentile; P95 = at 95^{th} percentile

Table 5. The sources, directions and magnitude of uncertainty related to dietary exposure assessment of tetracycline residues.

Sources of uncertainties	Direction and magnitude*
1. Representativeness of chicken meat sampling	++/--
2. Under or over reporting of consumed quantities	++/--
3. Limitation of children body weight	++/--
4. Change in chicken consumptions trends since 2014	+/-
5. Insufficient observed contamination data	+/-
6. Limitation of the analytical method	++

Note: *Key to direction and magnitude.
+, ++, +++ uncertainty likely to cause small, medium or large over-estimation of exposure
-, --, --- uncertainty likely to cause small, medium or large under-estimation of exposure

Probabilistic Analysis of the Dietary Tetracycline Exposure Assessment

Table 2, 3 and 4 show the estimated dietary intake of tetracycline from probabilistic analysis in terms of mean and percentiles. High percentile intakes, i.e., 90th and 95th were preferably included in the results to cover highly exposed individuals' intakes (EFSA, 2005). However, based on the ANOVA test, there is no significant difference among these three scenarios as $p<0.05$. Therefore, the discussion will focus on the higher bound scenario results summarized in Table 4. In general, tetracycline residues intake was higher in children (0.13779 µg/kg bw/day to 0.33935 µg/kg bw/day) compared to adults (0.04333 µg/kg bw/day to 0.09002 µg/kg bw/day). Based on Table 4, EDI for the children and adults could reach up to 0.16 % to 1.13 % and 0.12 % to 0.27 % of the defined ADI, respectively. These results are slightly higher in children and adults compared to previous data which were calculated through deterministic analysis as all possible data provided had been taken into account. The estimated risk between gender (men and women) and strata (urban and rural) revealed the same exposure pattern as calculated via deterministic analysis. Exposure to tetracycline residue were higher in men (0.04333 µg/kg bw/day to 0.09002 µg/kg bw/day) compared to women (0.03600 µg/kg bw/day to 0.07475 µg/kg bw/day) for higher bound scenario. The results are similar among strata which shows that people in urban area (0.04233 µg/kg bw/day to 0.08736 µg/kg bw/day) were exposed to tetracycline residue slightly higher compared to people in the rural area (0.03621 µg/kg bw/day to 0.07520 µg/kg bw/day). Among ethnicity, Chinese (0.03885 µg/kg bw/day to 0.08100 µg/kg bw/day) was exposed to the tetracycline more followed by Malay (0.03866 µg/kg bw/day to 0.08054 µg/kg bw/day) and Indian (0.02714 µg/kg bw/day to 0.05794 µg/kg bw/day). The intake patterns were similar as in deterministic calculation, but the exposure estimates were higher in probabilistic determination as all possible data are accounted for.

DISCUSSION

Deterministic Analysis

The estimated tetracycline intake of the lower bound may reflect underestimation of the intakes due to the fact that half LOD substituted the undetected samples. The medium bound scenario may reasonably designate a more realistic situation of estimated dietary intake of tetracycline on account of the non-detected data being replaced by LOD. However, the higher bound scenario results of estimated dietary intake of tetracycline were considered a worse-case scenario as MRLs replaced the non-detected samples. Thus, this scenario may tend to overestimate the dietary tetracycline intakes. However, from a one-way ANOVA test, the estimated dietary tetracycline intakes were not significantly different ($p>0.05$) among lower bound scenarios and medium bound scenarios, but they were significantly different ($p<0.05$) for higher bound scenarios. Therefore, the discussion will focus on the medium bound scenario, which is considered a more realistic situation of tetracycline intake, and the higher bound scenario, which is considered the worst-case scenario.

A dietary exposure assessment study on tetracycline residues through milk consumption carried out by Aalipour et al. (2015) discovered that the estimated daily intake of tetracycline residues for Iranian was roughly estimated to be a minimum 0.96 µg/kg bw/day (adult) to the maximum of 4.43 µg/kg bw/day (children), which were approximately 54 times higher for adults and 75 times higher for children compared to this study. Chicken meat is relatively low in cost compared to other protein sources with increases demands from consumers of higher income (Jayaraman *et al.,* 2013). This is because the chicken consumption rate is lower in Malay and Indian, as mean body weight for both are higher than the Chinese's mean body weight. However, there is no data available in the literature to compare with. In comparison, the exposure to tetracyclines from milk and meat was lower amongst Croatians, at 0.52 µg/person/day (Vragović *et al.,* 2011) and 0.7 µg/person/day (Vragović *et al.,* 2012), respectively. Another study done in the United States by the Environmental Protection Agency showed that the estimated exposure in oxytetracycline residues through milk consumption amongst Americans was 9.6 µg/person/day (USEPA, 2006) which is considered as low risk. That study findings are found to be higher compared to this study. The Food and Drug Administration also considered that this level should not be harmful to human health.

Overall, the results of estimated dietary intake of tetracycline from this study are considered low as the percentage of ADI for an adult is 0.1 % and for children is 0.2 % based on a higher bound limit (worst case), that does not exceed the ADI values of 30 µg/kg bw/day which is considered safe. According to JECFA (2006), the ingested chemical compound is considered acceptable if the estimated dietary intake calculated for that particular consumer is below the ADI or MRLs. However, since tetracycline residues may also be found in additional food sources, such as eggs, offal, milk and fish, the consumers may receive tetracycline residues at a level greater than the defined ADI if the tetracycline residues have contaminated several food sources (Aalipour *et al.,* 2015). Thus, a more refined estimation should be conducted in order to get a realistic determination of EDI for adults and children.

Probabilistic Analysis

Probabilistic analysis method provides more accurate information than the deterministic analysis as it considers different possible combinations of the contamination, consumption data, body weights as well as incorporating the correction factors. For this, the probabilistic method used all the above data distributions. In this regard, tetracycline concentration data, chicken consumption data, body weights and correction factors were best fitted to the pert distributions with three parameters: minimum, most likely (mean) and maximum.

Tables 2-4 show the estimated dietary intake of tetracycline from probabilistic analysis in terms of mean and percentiles. High percentile intakes, i.e., 90th and 95th were preferably included in the results to cover highly exposed individuals' intakes (EFSA, 2005). As in deterministic analysis, one-way ANOVA was performed in order to determine significant differences among those three scenarios. However, based on the ANOVA test, there is no significant difference among these three scenarios as $p<0.05$. Therefore, the discussion will focus on the higher bound scenario results summarized in Table 4.

Although the present study demonstrates that none of the investigated groups were exposed to the tetracycline residues at a level greater than the ADI at 30 μg/kg bw/day, the consumer may get 0.12 % to 1.13 % of the determined ADI by consuming chicken meat as the standard dietary recommended 14 g serving of chicken meat per day for children and chicken consumption amount for adults. The findings were lower than the study done by Aalipour et al. (2015) on the exposure estimation of tetracycline residue in adults and children from Iranians, whereby consumers may get 7 to 30 % off determined ADI via bovine milk consumption. Thus, the probabilistic analysis results imply that estimated dietary tetracycline exposure may not pose a risk to Peninsular Malaysia adult and children population. However, although the estimated dietary exposures to tetracyclines do not pose a risk to the populations, the exposure to tetracyclines residues are still there, calculated at around 1 %. According to Azad et al. (2014), this could lead to an increased risk of overweight cases among children, particularly children that are already exposed to the drugs in their first years of life. Since tetracyclines residues may also be found in other food sources (Aalipour *et al.,* 2015), it is beneficial to conduct proper surveillance in order to ensure unsafe foods are removed from the market and therefore not consumed by the public, especially major foods, as these might contribute most to exposure and thus lead to the greatest impact on the risk to the population.

Uncertainties Related to Dietary Tetracycline Exposure Assessment

A simple qualitative uncertainty table format recommended by EFSA guideline (EFSA, 2007) was followed and is illustrated in Table 5. Dietary exposure assessment uncertainty is due to limited knowledge about the data, data availability, and exposure indeterminacy (EFSA, 2007). As an integral part of dietary risk assessment, uncertainties in dietary exposure assessments are important and it is relevant to understand the results very well for correct interpretation (Kettler *et al.,* 2015). There are different sources of uncertainties inherent to exposure assessments. These may arise from concentration, consumption, and other factors determining exposures. Concentration data uncertainty would result from lack of representativeness of the analyzed food samples to all food considered in exposure assessment (Kroes *et al.,* 2002)

Representativeness of chicken meat sampling might result in over or underestimation of exposure. Since 2013, the number of slaughterhouses might have changed, whether it increased or decreased. The source of the chicken meat sample could be accurately designed for sampling when there is a proper and current list of chicken slaughterhouses made available. Thus, the number of contaminated chickens might increase or decrease and might not represent the whole number of slaughtered chickens in Peninsular Malaysia. This might also cause insufficient amounts of observed contamination data.

Underreporting or over-reporting would result from the applied method in food consumption data. This was observed in children's chicken consumption data since the reported value 14 g is based per meal, not g/day. The minimum and maximum chicken consumptions were based on the assumption that the children might eat the chicken (7 g) cooked together with fried rice or fried noodles and the children might eat the chicken (42 g) in every three common meals, which are breakfast, lunch and dinner, respectively. This will surely lead to underestimation or overestimation of dietary intakes, which in turn would result in under and over-estimating the exposure as well.

During the calculation of the dietary exposure, body weight is incorporated so that the exposure value practically represents the actual weight of that particular target group. However, the data applied for children's body weight are from international studies that are not specifically gathered from Malaysia or at least from Asian countries. The children's body weight for Malaysia or specifically from Peninsular Malaysia might be less, at par or more compared to the applied data. This might have probably caused an underestimation or overestimation of the dietary exposure calculations. The chicken consumption data for adults applied in this study were obtained from Institute for Public Health (IPH) (2014). Since then, the current year's food consumption pattern/intake might have changed. Therefore, these might have caused equally underestimation or overestimation of the dietary exposure to tetracycline residue intake.

The analytical method limitation was observed in LOD, where the LOD concentrations are quite high, almost half of MRLs. Hence, the replacement of undetected concentration data might have caused an overestimation of the exposure.

CONCLUSION

This study demonstrated that the dietary risk exposure of the Peninsular Malaysia consumers to antibiotic residues, particularly to tetracyclines residues in chicken meat from small and medium scale chicken slaughterhouses is low and the risk should not be neglected as consumers are predisposed to health hazards. The deterministic and probabilistic calculated dietary tetracycline intakes among children and adults in Peninsular Malaysia do not exceed relevant toxicological reference values (ADI), and therefore these chicken meats are safe for human consumption. The dietary tetracycline intake for both children and adults are almost 99 % lower than ADI 30 µg/kg in the worst-case scenario, even when the intakes of high consumers are considered. In order to ingest 30 µg/kg bw/day, children of 20 kg average body weight and an average adult weighing 67 kg would have to consume daily 6 kg and 20 kg of chicken meat containing tetracycline residues at the MRLs, respectively, in order to cause a risk.

REFERENCES

1. Aalipour, F., Mirlohi, M., Jalali, M., & Azadbakht, L. (2015). Dietary exposure to tetracycline residues through milk consumption in Iran. J. Environ. Health Sci. 13(1).

2. Azad, M. B., Bridgman, S. L., Becker, A. B., & Kozyrskyj, A. L. (2014). Infant antibiotic exposure and the development of childhood overweight and central adiposity. Int J Obes. 38(10): 1290–1298.
3. Cetinkaya, F., Yibar, A., Soyutemiz, G. e., Okutan, B., Ozcan, A., & Karaca, M. Y. (2012). Determination of tetracycline residues in chicken meat by liquid chromatography-tandem mass spectrometry. Food Addit Contam Part B: Surveillance Communications. 5(1): 45–49.
4. Committee, & Ministry. (2013). Malaysian Dietary Guidelines for Children and Adolescents.
5. Croubels, S., Daeseleire, E., De Baere, S., De Backer, P., & Courtheyn, D. (2004). Feed and Drug Residues. Encyclopedia of Meat Sciences. 2:1172–1187.
6. Darko, G., Mensah, J. K., Dapaah, S. S., & Odei, J. (2015). Estimated dietary exposure to veterinary residues in chicken and eggs. Int. J. Food Contam. 2(1).
7. EFSA. (2005). Opinion of the Scientific Committee on a request from EFSA related to A Harmonised Approach for Risk Assessment of Substances Which are both Genotoxic and Carcinogenic. 1–31.
8. EFSA. (2007). Guidance of the Scientific Committee on a request from EFSA related to uncertainties in dietary exposure assessment. 1–54.
9. International Law Book Services, (2015). Food Act 1983 (Act 281) and Food Regulations 1985. Retrieved from http://fsq.moh.gov.my/v6/xs/page.php?id=72.
10. Ronquillo, M. G., & Hernandez, J. C. A. (2017). Antibiotic and synthetic growth promoters in animal diets: review of impact and analytical methods. Food Control. 72: 255-267.
11. Institute for Public Health (IPH). (2014). National Health and Morbidity Survey 2014: MANS 3.
12. Jayaraman, S., Thangavel, G., Kurian, H., Mani, R., Mukkalil, R., & Chirakkal, H. (2013). Bacillus subtilis PB6 improves intestinal health of broiler chickens challenged with Clostridium perfringens-induced necrotic enteritis. Poult Sci. 92(2): 370–374.
13. JECFA. (2006). Updating the Principles and Methods of Risk Assessment : MRLs for Pesticides and Veterinary Drugs. In FAOUN.
14. Kettler, S., Kennedy, M., McNamara, C., Oberdörfer, R., O'Mahony, C., Schnabel, J., Smith, B., Sprong, C., Faludi, R., & Tennant, D. (2015). Assessing and reporting uncertainties in dietary exposure analysis. Mapping of uncertainties in a tiered approach. Elsevier Ltd. Food Chem. Toxicol 82: 79–95.
15. Kroes, R., Müller, D., Lambe, J., Löwik, M. R. ., van Klaveren, J., Kleiner, J., Massey, R., Mayer, S., Urieta, I., Verger, P., & Visconti, A. (2002). Assessment of intake from the diet. Food Chem. Toxicol. 40: 327–385.
16. Marzura, M. R., Nor Ainy, M., Ungku Fatimah, U. Z. A., Chai, L. C., Marni, S., & Khairunnisak, M. (2018). Occurance of tetracyclines, sulphonamides and quinolones residues in chicken meat sample from selected chicken slaughterhouses in Peninsular Malaysia. MJVR. 9(2): 88–101.
17. Salama, N. A., Abou-Raya, S. H., Shalaby, A. R., Emam, W. H., & Mehaya, F. M. (2011). Incidence of tetracycline residues in chicken meat and liver retailed to consumers. Food Additives and Contaminants: Part B Surveillance. 4(2): 88–93.
18. USEPA. (2006). Report of the food quality protection act (FQPA) tolerance reassessment progress and risk management decision (TRED) for oxytetracycline (Issue June).
19. Vragović, N., Bažulić, D., Jakupović, E., & Zdolec, N. (2012). Dietary exposure assessment of streptomycin and tetracycline in food of animal origin on the Croatian market. Food Addit Contam Part B Surveill. 5(4): 236–240.
20. Vragović, N., Bažulić, D., & Njari, B. (2011). Risk assessment of streptomycin and tetracycline residues in meat and milk on Croatian market. Food Chem. Toxicol. 49(2): 352–355.
21. Vutey, V., Baldias, L. R., Divina, B. P., & John Ducusin, R. T. (2012). Estimated maximum daily intake of streptomycin residue in pork consumed by age and gender groups in the Philippines. IJERD-International Journal of Environmental and Rural Development. 3(1): 62–67.

ACKNOWLEDGEMENT. This project was supported by the project entitled "Improvement of Safety, Quality and Traceability of Animal-based Food" (Reward: UPMCS-517) funded by the Department of Veterinary Services Malaysia. The authors also express their gratitude to the Veterinary Public Health Laboratory staff for facilitating this research.