British Journal of Medicine & Medical Research
13(12): 1-8, 2016, Article no.BJMMR.23306
ISSN: 2231-0614, NLM ID: 101570965

SCIENCEDOMAIN *international*
www.sciencedomain.org

Congenital Anomalies of the Alimentary Tract in Children: Experience in a Tertiary Health Facility in Enugu, Nigeria

Christopher Bismarck Eke[1*], Uchechukwu Obiora Ezomike[2], Bartholomew Friday Chukwu[1] and Nnamdi Benson Onyire[3]

[1]Department of Paediatrics, College of Medicine, University of Nigeria/University of Nigeria Teaching Hospital, Ituku- Ozalla, Enugu, Enugu State, Nigeria.
[2]Paediatric Surgery Unit, Department of Surgery, University of Nigeria Teaching Hospital, Ituku- Ozalla, Enugu, Enugu State, Nigeria.
[3]Department of Paediatrics, Ebonyi State University, Abakaliki, Ebonyi State, Nigeria.

Authors' contributions

This work was carried out in collaboration between all the authors. Author CBE conceptualized and designed the study, participated in the data collection/analysis and wrote the first draft of the manuscript. Authors UOE, BFC and NBO contributed in data collection/analysis and initial manuscript draft. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/23306
Editor(s):
(1) Toru Watanabe, Department of Pediatrics, Niigata City General Hospital, Japan.
Reviewers:
(1) Ramesh Gurunathan, Sunway Medical Center, Malaysia.
(2) Natasa Marcun Varda, University of Maribor, Slovenia.
Complete Peer review History: http://sciencedomain.org/review-history/13382

Original Research Article

Received 24th November 2015
Accepted 18th January 2016
Published 22nd February 2016

ABSTRACT

Background: Congenital anomalies including those of the alimentary tract are among the leading causes of childhood morbidity and mortality. A variety of these anomalies could affect the alimentary tract with various medical as well as economic costs. The aim of the current study was to determine the prevalence of the different forms, maternal as well as birth characteristics and outcomes of the congenital anomalies of the alimentary tract in hospitalized children in Enugu.
Methods: A 3 year retrospective audit of all hospitalized cases of alimentary tract anomalies was carried out. Case definitions of the different forms of alimentary tract anomalies studied were based on International Classification of Diseases and Related Problems, Tenth Edition (ICD-10). Data was

**Corresponding author: E-mail: christopher.eke@unn.edu.ng, chriseke2006@yahoo.com;*

analyzed using SPSS version 21.0 while level of statistical significance was set at $p<0.05$.
Results: A total of 59 children (37 males and 22 females) with alimentary tract anomalies were admitted during the period under review. Anorectal malformations 26(44.1%), Hirschsprung's disease 14(23.7%) and Ompalocoele 5(8.5%) were the most common anomalies observed. Congenital talipes equinovarus deformity of the lower limbs was the most predominant associated congenital anomaly. Maternal periconceptional use of herbal medications was reported in 7 (11.9) cases.
The case fatality rate was 5.1%.
Conclusion: A variety of alimentary tract anomalies do occur in children in our setting with some mothers having taken various forms of herbal medications in pregnancy. Efforts should be made to educate mothers on the need to avoid use of herbal concoctions during periconceptional period and in pregnancy as it could lead to a possible congenital anomaly.

Keywords: Alimentary tract; congenital anomalies; children; Nigeria.

1. INTRODUCTION

The alimentary tract is known to have a variety of congenital malformations, [1,2], arising mainly from – abnormal canalization (stenoses and atresias), duplications, malrotations and abnormal fixations, abdominal wall defects in addition to anomalies due to embryonic structural persistence (e.g. Meckel diverticulum) or abnormal formation of specific regions of the gastrointestinal tract (e.g. Microgastria) or its cellular components (e.g. neuroblasts in Hirschsprung's disease) [3-5].

The major congenital anomalies of the alimentary tract usually present with features of intestinal obstruction as well as effects on surrounding structures or its associated anomalies [1,3,4].

Majority of the causes of congenital anomalies in humans are not known. However, in about 25% of cases, multifactorial aetiologies have been implicated pointing to a complex interaction between genetic and environmental factors [6].

The World Health Organization (WHO) estimates that worldwide major congenital anomalies account for over 270,000 neonatal deaths annually (amounting to about 7% of all neonatal deaths) [7,8]. In addition these conditions add extra direct as well as indirect economic costs to both the parents as well as the healthcare systems that have been known to be weak in a background of limited resources as obtainable l in our setting.

Most of the countries in the sub-Saharan Africa may be unlikely to meet up with the realization of the Millennium Development Goal – four (MDG-4) aimed at reducing child mortality indices by this year 2015 due to the fact that they have recorded increasing proportion of neonatal mortality (from 10% to more than 40% of the overall under-five mortality) [9].

Major malformations are known to result in significant neonatal morbidity and mortality.

Few studies have been reported on the overall gastrointestinal tract congenital anomalies in Nigerian children [10], however there have been several studies in the various isolated alimentary tract anomalies [11,12].

Furthermore no similar study has been reported from the entire South Eastern Nigeria with an estimated total population of about 16.4 million people [13], (out of which children less 14 years constitute over 40% of the national total population). Many children delivered in our communities may be dying from complications of various forms of congenital malformations including those involving the alimentary tract.

This study therefore was aimed at determining the prevalence, pattern, risk factors and outcomes of children with congenital alimentary tract anomalies at the University of Nigeria Teaching Hospital, Enugu South East Nigeria.

2. METHODS

2.1 Study Area

The study was conducted at the Newborn Special Care Baby Unit (NBSCU) and Paediatric Surgical Ward of the University of Nigeria Teaching Hospital (UNTH), Ituku/Ozalla, Enugu. The NBSCU was established in 1975 to offer special care to at risk and ill newborn babies.

The hospital was then located at her temporary site within the Enugu metropolis.

It also has a very active Paediatric Surgical Unit with a Professor and three Consultant Paediatric Surgeons and senior registrars and registrars on rotational postings as well as supernumerary residents on training.

The NBSCU is currently staffed by a professor and three consultants, and 4 senior registrars, 4 registrars, 3 house-officers on continuous rotations and eighteen nurses. Facilities for incubator care, intubation, assisted ventilation, supplemental oxygen administration, phototherapy, apnoea monitoring and exchange blood transfusion are available in the unit in addition to other basic newborn services. Facilities for genetic testing are not available in our centre and are thus not offered to babies treated in the unit.

In January 2007, the hospital (UNTH) was re-located to its permanent site at Ituku/Ozalla, about 15 km away from the heart of Enugu metropolis.

2.2 Study Population

The NBSCU provides care for babies born within and outside the hospital and also receives referrals from different parts of Enugu, the rest of Enugu State and surrounding states of Abia, Anambra, Benue, Ebonyi, Delta, Imo and Kogi. Enugu State of Nigeria has a population of about 3 million people according to the national census of 2006 [14].

2.3 Study Design

This was a cross-sectional retrospective study in which an audit of the records of all newborns admitted in the Newborn Special Care Unit (NBSCU) and Paediatric Surgical wards of the UNTH, Enugu over a three year (2012-2014) period was carried out.

Ethical approval for the study was sought from the Health Ethics and Research Committee of the University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu, Nigeria.

The ward registers were reviewed to select all cases of congenital anomalies of the alimentary tract. The case files of the patients with these anomalies were retrieved from the medical records department and information including biodata, medical history and physical examination findings were retrieved. The maternal characteristics of the mothers were also obtained from the records.

Adequate antenatal care among mothers was defined as mothers that had at least four antenatal visits with an appropriate health care provider and receiving the recommended doses of the tetanus toxoid vaccination. The mother also needs support from her family and community in seeking care at the time of delivery and during the postpartum and lactation period. [15].

The case definition of the different cases of alimentary tract anomalies studied was based on their different standard definitions using ICD10 criteria [16].

The diagnosis, relevant investigation findings as well as treatment offered were recorded in a semi-structured questionnaire designed for this study. The treatment outcomes as at time of the review were also recorded. However, patients with incomplete data set were excluded.

The objectives of this study were to determine the prevalence; the different forms; birth as well as maternal birth characteristics and the outcome of the congenital malformations of the alimentary tract in children admitted at the Newborn Special Care Unit and Paediatric Surgical Unit of the UNTH, Ituku - Ozalla, Enugu.

Data collection was done with semi- structured forms designed for the study. Data was analyzed using SPSS version 21.0. Rates and proportions were calculated with 95% confidence intervals. The proportions were compared using *chi-square* with the level of significance was set at $P < 0.05$.

3. RESULTS

There were 37 (62.7%) males and 22 (37.3%) females diagnosed of congenital malformations of the alimentary tract. The median age at diagnosis was seven (7) days with a range of two hours to twelve years (25% percentile= 3 days, 75% percentile= 55.5 days) as presented in Table 1.

The maternal characteristics revealed a median age of 30 years with range of 18 years to 47 years at delivery of patients while most (35/59) of the mothers were between the ages of 27 years

and 33 years. Only 3.4% (2/59) were above 40 years.

Table 1. Demographic characteristics of study population and their caregivers

	Frequency N = 59	Percent (100%)
Age in months (Cases)		
0 – 7 days	34	57.6
8- 28 days	11	18.6
29 days – 12 months	7	11.9
13- 36 months	3	5.1
37 – 60 months	2	3.4
>60 months	2	3.4
Gender		
Male	37	62.7
Female	22	37.3
Maternal age		
<35years	51	86.4
35 years and above	7	11.9
Not indicated	1	1.7
Maternal education		
No formal education	0	0.0
Primary	9	15.3
Secondary	35	59.3
University/Polytechnic/ College of education	15	25.4

The majority (71.9%) of the mothers had adequate antenatal care. Although 18.6% (11/59) had no records of antenatal care, 11.9% (7/59) had irregular and inadequate care. Majority of the patients were delivered vaginally 49 (83.1%). Similarly 54 (91.5%) had adequate use of folic acid supplementation during pregnancy while 7 (11.9%) were exposed to various types of herbal medications in utero. Majority of the patients (94%) were delivered at term with normal birth weights. There was no associated family history of congenital anomalies in any of the patients as presented in Table 2.

A total of about 6317 paediatric admissions were recorded over the study period. Fifty nine of these were found to have anomaly of the alimentary tract of various types, giving a prevalence of 0.93%.

The prevalence of the various alimentary tract anomalies observed were as follows: anorectal malformations 0.41%, Hirschsprung disease 0.22%, omphalocoele 0.08%, cleft lip/palate 0.05%, duodenal atresia 0.05%, tracheo-oesophageal fistula 0.03%, achalasia 0.03%, jejunal atresia 0.03%, gastroschisis 0.02%, malrotation with midgut volvulus 0.02% respectively.

Table 2. Maternal birth characteristics and associated risk factors in children with alimentary tract congenital anomalies

Characteristic	Frequency N= 59	Percent
Mode of delivery		
Vaginal delivery	49	83.1
Caesarian section	7	11.9
Not indicated	3	5.1
Family history of birth deformities		
No	47	79.7
Yes	0	0.0
Not Indicated	12	20.3
Folic acid intake in pregnancy		
No	3	5.1
Yes	54	91.5
Not Indicated	2	3.4
Use of herbal medication		
No	44	74.6
Yes	7	11.9
Not Indicated	8	13.6

Recognized congenital anomalies of the alimentary tract were: anorectal malformations 26 (44.1%) Hirschsprung's disease 14 (23.7%), omphalocoele 5(8.5%), cleft lip/and or palate 3 (5.1%), duodenal atresia 3 (5.1%), tracheo - oesephageal fistula 2 (3.4%), jejunal atresia 2 (3.4%) achalasia of oesepahgus 2 (3.4%), among other as shown in Table 3.

Table 3. Distribution of alimentary tract congenital anomalies

Gastrointestinal anomaly	Frequency N = 59	Percent (100%)
Anorectal malformations	26	44.1
Hirschsprung's disease	14	23.7
Omphalocoele	5	8.5
Cleft Lip/Palate	3	5.1
Duodenal Atresia	3	5.1
Tracheo –Oesophageal Fistula (TOF)	2	3.4
Achalasia of Oesephagus	2	3.4
Jejunal Atresia	2	3.4
Gastroschisis	1	1.7
Malrotation with Midgut Volvulus	1	1.7

Associated anomalies were seen in four patients which included congenital talipes equinovarus deformity of the lower limbs in two patients (both males), a female with Downs facies who had duodenal atresia and presented with acute intestinal obstruction at birth and a case of esophageal anomaly who had associated cardiac anomaly.

All the 26 patients with anorectal malformations were essentially diagnosed clinically and with the aid of distal colostography in many of them distal anatomy was defined. Treatment of the cases of anorectal anomalies involved an initial defunctioning colostomy, corrective posterior sagittal anorectoplasty in about 21 cases while 17 have had the subsequent colostomy closure as at the time of this review.

Hirschsprung's disease cases had initial barium enema to identify the transition zone while the diagnoses were confirmed using full thickness rectal biopsy and histology. Treatment was by an initial colostomy in all cases while about 10 cases have had the subsequent pull through coloanal anastomosis.

One case of esophageal anomaly had associated cardiac anomaly and was being co-managed with the cardiothoracic Unit. Another case of tracheo- oesophageal fistula presented with pneumonia and severe acute malnutrition and was managed conservatively for the infections and weight gain optimization by feeding gastrostomy before surgery.

The two cases of the tracheo- oesophageal fistula (TOF) seen had definitive thoracotomy with oesophago-oesophagostomy, however one demised due to sepsis.

Plain x- ray depicted the typical double bubble appearance in the three cases of duodenal atresia while all had duodenoduodenostomy with good outcome.

A case of omphalocoele reported that had intact membrane was initially managed non-operatively, converting it into a ventral hernia that was subsequently repaired.

Outcomes of the paediatric alimentary tract congenital anomalies admissions under review were as follows: 52(88.1%) received different varieties of medical and surgical treatments; 4(6.8%) were discharged against medical advice (DAMA), while 3(5.1%) patients died, Of the mortalities, one each (1.7%) had gastroschisis and malrotation with midgut volvulus and a third with tracheo- oesophageal fistula died of severe sepsis giving a case fatality rate of 5.1%.

4. DISCUSSION

The present study has highlighted the prevalent cases and probable outcomes of alimentary tract congenital anomalies in children seen at the University of Nigeria Teaching Hospital, Enugu, Nigeria.

Few studies have been reported on the alimentary tract anomalies in children in Nigeria [10]. However, isolated cases of different alimentary tract malformations in children have been variously reported in our setting, [11,12] as well as general congenital anomalies in children [10,17-19].

Findings from the current study appear similar to a previous study by Falade and colleagues [10] in Ibadan, South West Nigeria. However, the latter was mainly on upper alimentary tract malformations.

The 0.93% prevalence reported in the present study though much lower than the 3-7% prevalence of overall congenital malformations in the general population, [8,20] is meant to create an awareness of the magnitude of the problem in our setting. As a tertiary hospital based study, it is likely that most of the cases of children with congenital alimentary tract anomalies born in the community could have passed on without being reported. So the present study could have under – reported the burden of the problem in our setting.

Maternal age and maternal educational backgrounds were not statistically related to the incidence of alimentary tract anomalies in the current study. However, studies have shown that maternal age above 35 years has been associated with the birth of children with congenital anomalies and that there is also a low incidence of having babies with congenital anomalies among mothers aged less than 20 years [21-23].

Low educational attainment could also be a reason for lack of proper antenatal care and non-compliance with the use of primary and secondary preventive measures of congenital anomalies. However, in the current study majority of the mothers had adequate basic education and optimal antenatal care.

A sizeable number of the mothers in the current study reported use of different types of herbal concoctions during pregnancy. Potentially almost any drug used in pregnancy could be teratogenic and about 2-3% of birth defects are due to exposure to certain drugs [24]. Also evidence has shown some associations of maternal use of

various forms of herbal medicine in early pregnancy and delivery of newborns with different forms of major congenital anomalies; [25,26] while some studies did not report any such associations. [27,28] Seven (11.9%) of the mothers in the current study made use of herbal medications in the first, second and/or third trimester(s) of pregnancy respectively. Amongst the "Igbo" ethnic nationality of south eastern Nigeria where the study was conducted there is this cultural belief that use of some herbal concoction as complementary or alternative medicine in pregnancy could help to make their babies to be "light" weight, thereby helping them to circumvent caesarean section delivery following prolonged obstructed labour. They believe that vaginal delivery is the pride of every woman and as such most women prefer to have vaginal delivery. Also some prospective mothers (women of child bearing age) could have been taking some herbal concoctions for the treatment of infertility without knowing when they became pregnant and apparently exposing their fetuses to the deleterious effects of such local herbal remedies early in intra- uterine life.

Adequate diagnosis of the different anomalies of the alimentary tract cases reported in the current study were done as our centre has different radiological services including x-rays, ultrasonography, computerized axial tomography scan, while magnetic resonance imaging is obtainable on private basis. Also there are no facilities for genetic studies at the moment. However the patients are given genetic counseling by a consultant paediatrician.

Affected children with different forms of alimentary tract anomalies received different forms of both palliative and corrective surgeries depending on the diagnosis and clinical state of the child.

In the present study, majority of the mothers were reported to have had adequate antenatal care as well as use of folic acid supplementation in pregnancy.

It is known that the amount of folic acid intake by a pregnant mother during peri- conceptional period reduces the risk of congenital anomalies [29-31]. However majority of cases of congenital anomalies are known to be idiopathic and even in about 25% of proven cases, the aetiology appears to be multifactorial. So even though most of the mothers in this present study could have used supplemental folic acid sufficiently, other probable causes including genetic as well as environmental factors like drugs including herbs, infections, maternal age above 35 years etc could have played some causal roles.

Sepsis was the most common direct probable cause of mortality among the subjects. This has been corroborated by Falade and colleague in Ibadan Nigeria [10]. It is possible that some of the cases particularly those with defective anterior abdominal wall such as omphalocoele and gastroschisis could easily be complicated by sepsis, patients transferred from private hospitals or primary health centres could also have had increased risk of infections hence increasing the likelihood of mortality in them.

5. CONCLUSION

In conclusion, congenital anomalies including those of the alimentary tract are common in our setting. Health education particularly on avoidance of use of herbal medications during peri- conceptional period should be encouraged to stern the rise in cases of congenitally malformed babies and save lives.

6. LIMITATIONS

The retrospective nature of the current study limited access to some mother and child pair information that could have been relevant in further discussion.

Similarly the study was not designed to capture data on periconceptional history of mothers who gave birth to normal children without alimentary tract/ or other congenital anomalies.

CONSENT

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Fotis L, Burns AJ, Thapar N. Gastrointestinal tract: congenital abnormalities. Available:http://www.wiley.com/doi.10:1002/9780 470015902.a0002138.pub2/ (Accessed: 5th July, 2015)

2. Hupta AK, Guglani B. Imaging of congenital anomalies of the gastrointestinal tract. Indian J Pediatr. 2005;75(s):403-414.
3. Martin V, Shaw-Smith C. Review of genetic factors in intestinal malrotation. Pediatric Surgical International. 2009;26(8):769-781.
4. Mclin VA, Hening SJ, Jamrich M. The role of the visceral mesoderm in the development of the gastrointestinal tract. Gastroenterology. 2009;136:2074-2091.
5. Mundt E, Bates MD. Genetics of Hirschsprung's disease and anorectal malformations. Seminars in Pediatric Surgery. 2010;19:107-117.
6. Moore KL, Persaud TVN. Human birth defects. In the developing human: Clinically oriented embryology. Philadelphia: Saunders; 2003;157-186.
7. World Health Statistics. Geneva World Health Organization; 2008.
8. Mashuda F, Zuechner A, Chalya PL, Kidneya BR, Manyama M. Pattern and factors associated with congenital anomalies among young infants admitted at Bugando Medical Centre, Mwanza, Tanzania. BMC Research Notes. 2014; 7:195.
   Available:http://www.biomedcentral.com/1756-0500/7/195
   (Accessed: 23rd July, 2015)
9. Richards V, Sanchez – uribe E, Esparza – Aguilar M, Esteves – Jaramillo A, Suarez – Iductah. Contribution of Mexico's universal immunization program to the fourth Millennium Development Goal. Rev Panam Salud Publica. 2014;35:248-255.
10. Falade AG, Shonubi AM. Pattern of congenital alimentary tract malformations in Ibadan, Nigeria. East African Medical Journal. 1997;74:385-388.
11. Adekunle OO, Johnson AOK. Congenital anorectal anomalies in Western Nigeria. Niger J Paed. 1981;8:40-44.
12. Olajide AL, Yisau AA, Abdulraseed NA, Kashim IOO, Olaniyi AJ, Morohunfade AOA. Gastrointestinal duplications: experience in seven children and a review of the literature. The Saudi Journal of Gastroenterology. 2010;16:105-109.
13. The 2006 Nigeria Census figures.
   Available:http://www.nigeriaworld.com/articles/2007/jan/112.html
   (Accessed: 12th June, 2015)
14. Enugu State – National Population Commission
   Available:http://www.population.gov.ng/index.php/enugu-state
   (Accessed: 14th December, 2014)
15. World Health Organization. Child health and development: Antenatal care.
   Available:www.emro.who.int/child-health/community/family-practices/antenatal-care
   (Accessed: 19th November, 2015)
16. World Health Organization. International Statistical Classification of Diseases and Health problems, 10th ed. 2010.3r.
   Available:http://www.int/classifications/icd10/browse/content/statichtml/ICD10Volume2_en_2010.pdf
   (Last Accessed: 20th November, 2012)
17. Ekwere EO, McNail R, Agim B, et al. A retrospective study of congenital anomalies presented at tertiary health facilities in Jos, Nigeria. JPCS. 2011;3:24-28.
   Available:http://www.arpapress.com/volumes /JPCS/Vol3/JPCS_3_03.pdf
   (Accessed: 28th September, 2014)
18. Onyearugha CN, Onyire BN. Congenital malformations as seen in a secondary healthcare institution in Southeast, Nigeria. J Med Investig Pract. 2014;9:59-62.
   Available:http://www.jmip.org/text.asp?2014/a/59/139163
   (Accessed: 20th July, 2015)
19. Obu HA, Chinawa JM, Uleanya ND, Adimora GN, Obi IE. Congenital malformations among newborns admitted in the neonatal unit of a tertiary hospital in Enugu, South East, Nigeria – A retrospective study. BMC Research Notes. 2012;5:177.
   Available:http://www.biomedcentral/com/1756-0500/5/177
   (Accessed: 21st June, 2015)
20. Sekhobo JP, Druschel CM. An evaluation of congenital malformations surveillance in New York State: An application of Centers for disease control and prevention (CDC) guidelines for evaluating Surveillance Systems. Public Health Rep. 2000;116: 296-305.
   DOI: 10.1016/SOO33-3549(04)50051-1
21. TNSA 2003, Hacettepe University, Institute of population studies and Macro-International Inc. Turkish Demographic and Health Survey (dhs-2003); 2003.
   Available:http://www.hips.hacettepe.edu.tr/tnsa2003/anarapor-english.httm
   (Accessed: 3rd January 2006)

22. Mohamed A, Mohamed M, Ahmed E, Wael B. Dysmorphogenesis, clinical study. Ass. Univ. Med. J. 2007;30:159-184.
23. Silvana G, Mavia D. Congenital malformations in Rio de Janeiro, Barzil: prevalence and associated factors. Cad. Saude Public Rio de Janeiro. 2006;22: 2423-2431.
24. Niebyl JR, Simpson JL. Teratology and drugs in pregnancy. In: The Global library of women's medicine; 2008.
DOI: 10.3843/glowm.10096
Available:http://www.glown.com/section_viewleading/teratology%20ands%20drugs%20inpregnancy/
(Accessed: 4th August, 2014)
25. Chuang CH, Doyle P, Wang JD, Chamg PJ, Lai JN, Chen PC. Herbal medications used during the first trimester and analysis of data from a pregnancy cohort study. Drug Saf. 2006;29:537-548.
26. Osaghae DO, Mukwuzi – Odum LN, Edobor E, Enukegwu SN. Risk factors in the development of prune belly in a Nigerian child. Journal of Medicine and Medical Sciences. 2012;3:443-446.
27. Hoist L, Nordeng H, Haavik S. Use of herbal drugs during early pregnancy in relation to maternal characteristics and pregnancy outcomes. Pharmacoepidemiol Drug Saf. 2008;17(2):151-159.
28. Heitmann K, Nordeng H, Hoist L. Pregnancy outcome after use of cranberry in pregnancy- the Norwegian mother and child cohort study. BMC Complement Altern Med. 2013;13:345.
DOI: 10:1186/1472-6882-13-345
29. Jiang X, Xu G, Shen L, Wu J, Chen H, Wang Y. Influential factors on congenital gastrointestinal malformation: A hospital_based_control study. Zhonghua Liu Xing Bing Xue Zn Zhi. 2014;35:81-84.
30. QueiBer-Luft A, Spranger J. Congenital malformations. Dtsch Arztebl. 2006;103: A2464-A2471.
31. Little J, Cardi A, Arslan MT, Gilmour M, Mossey PA. Smoking and orofacial clefts: a United Kingdom_based case_control study. Cleft Palate Craniofacial Journal. 2004;4:381-386.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/13382