CESAREAN IN ADOLESCENTS AT THE RURAL HOSPITAL OF NEISU (Democratic

Republic of Congo): Epidemiological aspects and neonatal and maternal

- 3 **prognosis.**
- 4 Abstract

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- 5 Aim: we attempted to determine the epidemiological aspect of cesarean section performed in
- 6 adolescent girls at Neisu Rural Hospital, DR Congo, and maternal and neonatal prognosis,
- 7 whereby to contribute to the reduction of maternal and neonatal morbidity and mortality.
- 8 **Methods**: Descriptive cross-sectional study from January ^{1st}, 2016 to June 30th 2018,
- 9 involving 114 cases of caesarean section of 13 to 19 year-olds. Maternal and perinatal data
- were analyzed on the SPSS 20.0 software
- 11 **Results:** The prevalence of caesarean section among adolescents was 24.8%. The majority
- of female deliveries had a low level of education (80.7%), half were married, 30.7% were
- transfer cases, 77.2% were primiparous, and 100% christian and 81.6% had not followed
- quality prenatal consultations. Cesarean section was done in emergency (97.4%) under spinal
- anesthesia (69.3%) and especially indicated for feto-pelvic disproportion (69.3%). In
- newborns there was: 1.8% of prematurity; 21.1% of low weight; 14.9% of resuscitation;
- 17 3.5% of Apgar <7 in the 5th minute; 9.6% of neonatal infection and 43.9 ‰ perinatal
- mortality. Concerning the maternal prognosis: 10.5% of severe anemia; 16.7% of parietal
- infection; 16.7% endometritis and 8.8% of maternal mortality.
- 20 **Conclusion**: The cesarean section in adolescent girls to Neisu is a public health problem
- and the fetal-maternal prognosis is worrying.
- 22 **Keywords**: Caesarean section, adolescent, DRC, Neisu.

23 INTRODUCTION

- 24 The guidelines of the World Health Organization (WHO) use the expression "early
- pregnancy" to characterize any pregnancy that occurs before the age of 20 [1]. Early and
- unwanted pregnancy is a global problem affecting both developed and developing countries.
- 27 It has a major impact on the lives of adolescents, especially girls, in many ways: health,
- social, economic and educational. Low- and middle-income countries have the highest
- 29 number of pregnant adolescents. In 36 of these countries, up to 25 per cent of girls between
- 30 the ages of 15 and 19 are either pregnant or already mothers, and in 16 low- and middle-
- income countries more than 40 per cent of girls marry before the age of 18 [2].

- 32 The situation with regard to early and unwanted pregnancies varies from one region to
- another and presents specificities related to the context of the different regions. For example,
- while Latin America, the Caribbean, and high-income countries have high rates of teenage
- out-of-wedlock pregnancies, in South Asia the majority of teenage pregnancies occur as part
- of a marriage or a free union. Sub-Saharan Africa has high rates in both scenarios (WHO,
- 37 2012). While early and unwanted pregnancies among young people are observed in a wide
- variety of settings, the critical issue is limited access to education and health services, as well
- as poor health outcomes [3].
- 40 Sub-Saharan Africa has the highest fertility rates among girls aged 15-19 (with 103 births per
- 41 1,000 girls), followed by Latin America and the Caribbean (64.57 births per 1,000 girls) (open
- data from the World Bank). In a 2015 study conducted in six countries (Kenya, Zambia, India,
- Pakistan, Guatemala and Argentina), the rate of adolescent pregnancy ranged from 2% in
- Pakistan to 26% in Argentina and the adolescent pregnancy among minors age 15 was
- observed only in sub-Saharan Africa and Latin America [2].
- 46 The evolution of teenage pregnancy is peppered with the psycho-social, economic and
- 47 biological consequences as well as its implication in maternal and fetal morbidity and
- 48 mortality [9]. Maternal complications during childbirth are made of the cephalo-pelvic
- 49 disproportion (which is often the indication of caesarean section), to stop labor, postpartum
- 50 hemorrhage is complicated by anemia, vesico-vaginal fistula [10] and tearing of the soft parts
- 51 if the episiotomy is not performed [11,12]. Among their newborns, there is a high rate of low
- birth weight, premature delivery, respiratory distress, various neonatal complications, and
- 53 perinatal mortality [4,9,13-16]. We conducted this study to determine the epidemiological
- 54 aspect of cesarean delivery in adolescent girls at Neisu Rural Hospital and maternal and
- 55 neonatal prognosis

DELIVERY AND METHODS

- 57 This descriptive cross-sectional study was conducted at the Notre Dame de Consolata
- 58 Hospital of Neisu (NDCHN). The NDCHN is a reference hospital, located in the village
- Neisu, 30 km from the town of Isiro, in the Haut-Uele province, North-East of the Democratic
- 60 Republic of Congo (DRC). Data collection was retrospective. Indeed, the documents analyzed
- were the mothers' consultation cards, the birth and the operating theater registers. During the
- 62 period of two years and six months (from 1st January 2016 to 30 June 2018), we collected a
- total of 460 deliveries for teenagers aged 13 to 19, including 114 cases of cesarean section.

- We have divided these teenagers into two age groups to allow us to identify the differences
- between them. Those aged 13 to 15 were considered young teenagers, and those aged 16 to 19
- as older teenagers. In the category of young teenagers, we recorded 114 deliveries, including
- 12 cesareans, and in the group of old teenagers we collected 346 deliveries including 102
- 69 cesareans.

- 70 Cases included in this study were those who met the inclusion criteria below:
- Have an age ranging from 13 to 19 years on the day of delivery and have delivered by
- 72 caesarean section to the NDCHN
 - Medical file duly completed and with the necessary elements for the study.
- 74 The collected data was captured and processed using the SPSS 20.0 software.
- 75 The following parameters were analyzed:
- 76 For the mothers:
- The socio demographic data : age (13-15 years and 16-19 years), level of instruction
- 78 (illiterate, primary, secondary and higher), marital status (married and single) and religious
- 79 denomination (Christian and other),
- Antecedents : parity (primiparous = 1 and secondiparous = 2), antenatal control (ANC)
- and history of caesarean section;
- 82 Progress of cesarean section : gestational age on day of caesarean section (28 to 36
- weeks, 37 to 42 weeks), indications for caesarean section, complications recorded.
- 84 For newborns : prognosis elements (Apgar at 5th minute, birth weight, neonatal infection
- and perinatal mortality).

87 **RESULTS**

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Prevalence of cesarean section in adolescent girls

- From 1st January 2016 to 30 June 2018, out of a total of 460 teen deliveries, we recorded 114
- 90 cases of cesarean section, which represents a prevalence of 24.8%. Taking into account the
- age categorization in this study, this prevalence was 10.5% among 13-15 year-olds and 29.5%
- 92 among 16-19 year-olds.

Sociodemographic characteristics

- 94 The sociodemographic characteristics are shown in Table I below. The average age of these
- cesarean section operations was 17.50 ± 1.2 years (range: 13 to 19 years) and they were all
- 96 Christian (100%). The majority (75.4%) of them had a primary education level, with 91.7% of

young teenagers and 73.5% of older teenagers. 53.9% of older teenagers were married compared to 16.7% of young adolescents.

 Table I : Sociodemographic characteristics

	13-15 years (n = 12)		16-19 years old (n = 102)		Total (N = 114)		
	Frequency	%	Frequency	%	Frequency	%	
Level of stud	y						
Illiterate	-	-	6	5.9	6	5.3	
Primary	11	91.7	75	73.5	86	75.4	
Secondary	1	8.3	21	20.6	22	19.3	
Marital statu	S						
Married	2	16.7	55	53.9	57	50.0	
Single	10	83.3	47	46.1	57	50.0	

Gynecological and obstetrical history

Among our patients, 77.2% were primiparous, 75.5% of young vs 91.7% of older teenagers. The majority of patients had followed ANC. In fact, 60% of older teenagers vs. 55% of young teenagers had attended 1-3 sessions of ANC. However, 33.3% of young teenagers had 4 or more sessions of ANC vs 16.7% of older teenagers. Caesarean section history was recorded only among older teenagers.

Table II: Gynecological and Obstetrical History

	13-15 years (n = 12)		16-19 yea	rs old	Total (N = 114)		
			(n=10)2)			
	Frequency	%	Frequency	%	Frequency	%	
Parity							
Primiparous	11	91.7	77	75.5	88	77.2	
Secondiparous	1	8.3	25	24.5	26	22.8	
Gestational ag	e (weeks)						
28-36	0	0	2	2.0	2	1.8	
37-42	12	100.0	100	98.0	112	98.2	
Antenatal con	trol						
0	3	25.0	30	29.4	33	28.9	
<4	5	41.7	55	53.9	60	52.6	
≥ 4	4	33.3	17	16.7	21	18.4	
History of Cae	esarean sectio	n					
None	12	100.0	84	82.3	96	84.2	
1	0	0	17	16.7	17	14.9	

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Indications and course of cesarean section.

Of all our patients, 35 (30.7%) were admitted with a transfer note and 69.3% without transfer. At admission, 100% of young teenagers had a term pregnancy against 98% of older teenagers. Caesarean section was performed urgently in 111 adolescents (97.4%) and programmed in 3 of them (2.6%). All caesareans performed in young teenagers girls were performed urgently. Before performing the caesarean section, the patient's examination had objectified rupture of the membranes in 10.5% of cases. Spinal anesthesia was performed in 69.3% and general anesthesia with Ketamine in 30.7% of cases. The technique of Misgav Ladach was performed in 89.5% of cases and the classic cesarean section by median incision under umbilical in 10.5% of cases. The latter technique was indicated only in patients who had a previous history.

The different indications for caesarean section for our patients are shown in Table 3. It was mainly cephalo-pelvic-disproportion (69%), acute fetal distress (35.1%), narrowed pelvis (21.9%), %), scar uterus (14.0%) and prolonged labor (13.2%). From these indications, cephalo-pelvic disproportion and extended labor predominated in young teenagers,

Table 3. Indications for cesarean section

	13-15 years		16-19 years old		Total	
	(n=12)		(n = 102)		(N = 114)	
	Frequency	%	Frequency	%	Frequency	%
Cephalo-pelvic disproportion	11	91.7	68	66.7	79	69.3
Acute fetal distress	3	25	37	36.3	40	35.1
Shrinked pelvis	2	16.7	23	22.5	25	21.9
Scarred uterus	0	0	16	15.7	16	14.0
Extended labor	2	16.7	13	12.7	15	13.2
Vicious presentation	0	0	10	9.8	10	8.8
Pre/uterine rupture	0	0	6	5.9	6	5.3
Dynamic dystocia	0	0	4	3.9	4	3.5
Eclampsia	0	0	1	1.0	1	0.9

respectively 91.7% and 16.7% vs. 66.7% and 12.7%, respectively, among older teenagers.

- We had registered 53.5% (61/114) of complications in newborns. Twenty four (21.1%)
- newborns had a low birth weight (8.3% for the young teenagers and 22.5% for the older
- teenagers) and two were premature (1.8%). At birth, 14.9% were resuscitated and at the 5th
- minute, four of them (3.5%) had an Apgar <7. There were 11 cases of neonatal infection, or
- 9.6% (16.7% among young teenagers and 8.8% among older teenagers). Neonatal mortality
- was 43.9 for 1000 birth (5/114).
- Maternal complications were recorded in 44.7% (51/114) of the cases. Indeed, the maternal
- prognosis was altered by 10.5% of severe anemia that required blood transfusion (8.3% in
- young teenagers and 10.8% in older teenagers), 16.7% of postoperative wall infection and
- 135 16.7% endometritis. Maternal mortality accounted for 8.8 for 1000 birth (1/114), only in the
- group of adolescent girls aged between 16 and 19 years.

DISCUSSION

- In our study, the prevalence of caesarean section is 24.8% (10.5% among young teenagers and
- 29.5% among older teenagers). This prevalence is higher to many series in the literature. This
- is the case of 19.8% in Turkey (with 15.3% among young teenagers and 20.1% among older
- teenagers) [17], 18.5% in Mozambique [18], 14%, 8% in Cameroon [11]. The same is true of
- an African multicenter study conducted in 2013 (in Algeria, Angola, DRC, Kenya, Niger and
- Nigeria) where Ganchimeg [16] found a prevalence of 11.4% among young teenagers and
- 145 9.1% among older teenagers.
- Ganchimeg [16] and Mombo-Ngoma [21] associate this variability with sociocultural and
- religious differences. We believe that our result will be due to the geographical location of
- this rural environment, the low level of education of our respondents, early marriage (a value
- in this community), poverty, lack of awareness about the prevention of pregnancy and the
- 150 lack of a contraceptive program in this environment. These justifications corroborate the
- prevalence recorded in our country by studies conducted in urban areas. Indeed, Akilimali
- 152 [19] recorded 12.8% of cases in 2015 in the city of Matadi and Xavier Kinenkinda found 10%
- of cases in 2017 at Lubumbashi [20].
- With regard to sociodemographic characteristics, the age of our respondents ranged from 13
- to 19 years with an average age of 17.50 ± 1.2 years. The majority of them (75.4%) had a
- primary education level, with 91.7% of young teenagers and 73.5% of older teenagers. 53.9%
- of older teenagers were married compared to 16.7% of young teenagers. Several other studies
- 158 conducted in rural areas found that pregnant teenagers had a low level of instruction [4,16,21].

- In Cameroon in 2015, Thomas Obinchemti Egbe [22] found in urban areas that the majority
- of teenagers who delivered by cesarean section (73.6%) had a secondary level of instruction.
- In our series, a total of 50% of teenagers girls were married. This proportion of brides was
- 162 16.7% among young teenagers and 53.9% among older teenagers. These results are similar to
- those of Ganchimeg [16], who also found 46.9% of brides among young teenagers and 62.9%
- of older women. Indeed, early marriage is a real problem in sub-Saharan Africa and has the
- 165 consequence of early pregnancy.
- In Cameroon, Florent Ymele Fouelifack [11] found 20.6% of pregnant teenagers brides and
- Thomas Obinchemti Egbe [22] found 58.7%. The difference with our results can partly be
- explained by the difference of the religious confessions. In our study, 100% of teenager girls
- were Christian. In the Thomas Obinchemti Egbe series [22], however, 95.9% of teenage girls
- operated for cesarean section were Muslim. Indeed, the radicalism of religious laws protects
- muslim girls to conceive at the age of majority and in marriage.
- 172 In our study, 60% of old teenagers vs. 55% of young teenagers had followed 1 to 3 sessions of
- ANC. However, 33.3% of young teenagers had 4 or more sessions of ANC vs 16.7% of older
- teenagers. In the study by Thomas Obinchemti Egbe [22], 59.5% of teenagers had followed 1
- to 3 ANC. Ganchimeg [16] found that pregnant adolescents in Africa often neglect ANC.
- Pregnancy during adolescence in our environment is often lived in hiding, it is therefore in the
- majority of cases poorly followed.
- The main indications for caesarean section performed in adolescent girls in this study were
- cephalo-pelvic disproportion (69%), acute fetal distress (35.1%), shrunken pelvis (21.9%),
- scarred uterus (14.0%) and extended labor (13.2%). Of these indications, cephalo-pelvic
- disproportion and extended labor had predominated among young teenagers, respectively
- 91.7% and 16.7% vs. 66.7% and 12.7% respectively among older teenagers. These findings
- are consistent with that of Ganchimeg [16] who also found cephalo-pelvic disproportion as
- the main indication for caesarean section for adolescents under 15 years of age.
- We had registered 53.5% of complications in newborns. In fact, 3.5% of newborns had a low
- Apgar (<7) in the 5th minute. This complication was observed in 4% of cases by Thomas
- Obinchemti Egbe [22]. In the Ingvil study [23], 13.5% of newborns of teenagers had an Apgar
- 188 <7 vs. 8.6% of cases in adult mothers.
- Low birth weight was reported in 21.1% of newborns, with predominance among older
- teenagers (8.3% among young teenagers vs 22.5% among older teenagers). Ganchimeg [16]
- had found the predominance of low weight among young teenagers. Mombo-Ngoma [21]
- found a total of 10% low birth weight (16% of adolescents under 16) and Thomas Obinchemti

- Egbe [22] found 9.5%. Beyond low maternal weight, we should also associate the share of malaria in the occurrence of low birth weight among teenage mothers in our environment.
- 195 Guyatt HL [24] found that in areas with high malaria transmission, Plasmodium infestation is
- responsible for 19% of low birth weight. It is also established that the impact of malaria is
- more pronounced during the first pregnancy [25].
- 198 We recorded 1.8% of prematurity among teenagers aged 17 to 19 years old. On the other
- hand, Oya Demirci [17] found that it was the young teenagers who gave birth prematurely.
- Our results converge with those of Mombo-Ngoma [11] and Florent Ymele Fouelifack [21]
- who found respectively 29.3% and 4% of premature teenage girls. The majority of authors
- 202 [16,24,25] have proved the relationship between young mothers on the one hand and low birth
- weight and prematurity on the other.
- We noted in this study that perinatal mortality rises to 43.9 for 1000 (43.9 %) birth, only in
- 205 the group of older teenagers. This result is higher than that of Fernando Althabe [4] in 2015
- 206 (34.2 %) in 6 countries in Sub-Saharan Africa and Latin America. In Cameroon, Thomas
- Obinchemti Egbe [22] had found 94.6 ‰ and Ganchimeg [16] found 76 ‰ among teenagers
- under 15 years and 50 % among those aged 16 to 19 years.

- 210 A study conducted in 4 countries in sub-Saharan Africa (Benin, Gabon, Mozambique, and
- 211 Tanzania) found on 2016 that low birth weight and prematurity were associated with early
- 212 maternal age [21].
- 213 The maternal prognosis was marked by the occurrence of complications in 44.7% of cases. In
- fact, 10.5% of teenage girls operated for cesarean section had experienced severe anemia and
- were transfused. For Fernando Althabe [4], there is no association between early age and
- antepartum haemorrhage; postpartum haemorrhage, labor stoppage, sepsis and hypertensive
- disorders. Beyond the blood loss recorded during the caesarean section, we believe that, being
- 218 in a malarial endemic area, these teenagers would have a low hemoglobin level before
- cesarean section.
- There was 8.8 % (8.8 for 1000 birth) of maternal mortality among teenagers aged 16 to 18
- years. Fernando Althabe [4] found 0.79 % while Ganchimeg [16] found 7.3 % among young
- adolescents and 2.9 ‰ among those aged 16-19.

- 224 CONCLUSION
- 225 The risks of maternal and perinatal mortality are more pronounced in Africa among
- adolescent girls than adults. This variability in perinatal and maternal mortality rates may

227	depend on each region, the socio-demographic characteristics of the gestants, the follow-up of
228	ANC, the competence of the health care staff to transfer on time, the geographical distribution
229	of the health structures as well as their technical platform.
230	
231	Conflicts of interest.
232	The authors declare that they have no conflict of interest in the writing of this article.
233	Ethical
234	NA
235	Consent
236	NA
237 238	
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REFERENCES

- 1. OMS. Les lignes directives sur la prévention de la grossesse précoce. www.who.int/maternal child adolescent/documents/preventing early pregnancy/en
- 2. OMS. *La santé des populations: les mesures efficaces*. Le rapport sur la santé dans la Région africaine. Bureau régional d'Afrique. 2014
- 3. UNESCO. Objectifs de développement durable : Grossesses précoces et non désirées.

 Recommandations à l'usage du secteur de l'éducation. Edition 2017. Sur

 www.unesco.org/aids
- Fernando Althabe, Janet L Moore, Luz Gibbons, et al. Adverse maternal and perinatal outcomes in adolescent pregnancies: The Global Network's Maternal Newborn Health
 Registry study. *Reproductive Health* 2015, 12(Suppl 2):S8
- 5. Nditsheni J. Ramakuela, Tsakani R. Lebese, Sonto M. Maputle, Lindiwe Mulaudzi . Views of teenagers on termination of pregnancy at Muyexe high school in Mopani District, Limpopo Province, South Africa. *Afr J Prm Health Care Fam Med.* 2016; 8(2), a945. http://dx. doi.org/10.4102/phcfm.
- Sarka Lisonkova, Matthew D. Haslam, Leanne Dahlgren et al. Maternal morbidity and
 perinatal outcomes among women in rural versus urban areas. *CMAJ* 2016.
 DOI:10.1503 / cmaj.151382.
- 7. J. Lansac, P. Descamps et J-F. Oury. Pratique de l'accouchement. 5è Edition, Masson, Paris, 2011.
- 8. Elizabeth Wall-Wieler, Leslie L. Roos and Nathan C. Nickel. Teenage pregnancy: the impact of maternal adolescent childbearing and older sister's teenage pregnancy on a younger sister. *BMC Pregnancy and Childbirth* (2016) 16:120
- 9. Walter Fernandes de Azevedo, Michele Baffi Diniz, Eduardo Sérgio Valério Borges da Fonseca, et al. Complications in adolescent pregnancy: systematic review of the literature. *Einstein* 2015;13(4):618-26
- 10. Demetra-Gabriela Socolov, Magdalena Iorga, Alexandru Carauleanu, et al. Pregnancy during Adolescence and Associated Risks: An 8-Year Hospital-Based Cohort Study (2007–2014) in Romania, the Country with the Highest Rate of Teenage Pregnancy in Europe. Hindawi Publishing Corporation. *BioMed Research International* Volume 2017, Article ID 9205016, 8 pages.
- 11. Florent Ymele Fouelifack, Theodore Yangsi Tameh, Eta Ngole Mbong et al. Outcome
 of deliveries among adolescent girls at the Yaoundé central hospital. *BMC Pregnancy and Childbirth* 2014, 14:102

- 12. Oya Demirci, Ertğrul Yılmaz, Özgür Tosun, et al. Effect of Young Maternal Age on
 Obstetric and Perinatal Outcomes: Results from the Tertiary Center in Turkey.
 Perinatal Medicine, 23-25 April 2015, İstanbul, Turkey.
- 13. João Luiz Pinto e Silva, Fernanda Garanhani Surita. Pregnancy in Adolescence A
 Challenge Beyond Public Health Policies. *Rev Bras Ginecol Obstet* 2017; 39(02): 041 043
- 14. <u>Leftwich HK</u>, <u>Alves MV</u> Adolescent Pregnancy. <u>Pediatr Clin North Am.</u> 2017 Apr;
 64(2):381-388. doi: 10.1016/j.
- 15. <u>Narukhutrpichai P, Khrutmuang D, Chattrapiban T</u>. The Obstetrics and Neonatal Outcomes of Teenage Pregnancy in Naresuan University Hospital. *J Med Assoc Thai*. 2016 Apr; 99(4):361-7.
- 16. T Ganchimeg, R Mori, E Ota, et al. Maternal and perinatal outcomes among nulliparous adolescents in low- and middle-income countries: a multi-country study.

 BJOG 2013; 120:1622–1630.
- 17. Oya Demirci, Ertğrul Yılmaz, Özgür Tosun, et al. Effect of Young Maternal Age on Obstetric and Perinatal Outcomes: Results from the Tertiary Center in Turkey. Perinatal Medicine, 23-25 April 2015, İstanbul, Turkey.
- 18. Qian Long, Taina Kempas, Tavares Madede et al. Caesarean section rates in Mozambique. *BMC Pregnancy and Childbirth* (2015) 15:253
- 19. Akilimali PZ, Nzau NE, Urbano P et al. The predictors of cesarean delivery in Kinkanda reference general hospital at Matadi (DR. Congo). *Mali Medical* 2015 Tome XXX N°2.
- 20. Xavier Kinenkinda, Olivier Mukuku, [...], et Justin Kizonde. Risk factors for maternal and perinatal mortality among women undergoing cesarean section in Lubumbashi, Democratic Republic of Congo II. *Pan Afr Med J.* 2017; 26: 208.
- 21. Mombo-Ngoma G, Mackanga JR, González R, et al. Young adolescent girls are at high risk for adverse pregnancy outcomes in sub-Saharan Africa: an observational multicountry study. *BMJ* Open 2016; 6: e011783. doi:10.1136/bmjopen-2016-011783
- 22. Thomas Obinchemti Egbe, Amadeus Omeichu, Gregory Edie Halle-Ekane et al.
 Prevalence and outcome of teenage hospital births at the Buea health district, South
 West Region, Cameroon. *Reproductive Health* (2015) 12:118
- 23. Ingvil K Sørbye, Siri Vangen, Olola Oneko et al. Caesarean section among referred
 and selfreferred birthing women: a cohort study from a tertiary hospital, northeastern
 Tanzania. BMC Pregnancy and Childbirth 2011, 11:55
- 24. Guyatt HL, Snow RW. Impact of malaria during pregnancy on low birth weight in sub-Saharan Africa. *Clin Microbiol* Rev 2004; 17:760–9.
- 25. Desai M, ter Kuile FO, Nosten F, et al. Epidemiology and burden of malaria in pregnancy. *Lancet Infect* Dis 2007; 7:93–104.

