

Pregnancy following Cardiac Surgery

S. Z. Bhutta, S. Aziz, R.Korejo

Department of Obstetrics and Gynaecology, Jinnah Postgraduate Medical Center, Karachi.

Abstract

Objective: To determine the pregnancy outcome in women with cardiac disease who have undergone cardiac surgery.

Design and Setting: Prospective study in a tertiary care hospital.

Population: One hundred and thirteen pregnant women who had cardiac surgery due to valvular disease (commissurotomy as well as valve replacement), or other cardiac defects. These women were followed up in 170 pregnancies between January 1990 and December 1999.

Results: Rheumatic heart disease (91%) affecting the mitral valve, was the commonest indication for cardiac surgery (89%). Valve replacement with mechanical prostheses followed by anticoagulant therapy was carried out in 45%. There was no maternal death. Maternal morbidity from complications included pulmonary oedema (16%), cardiac arrhythmias (4%), postpartum haemorrhage (3.5%). Other bleeding complications included epistaxis and haematoma at episiotomy site (2%). Impaired functioning of prosthesis (4%), severe pregnancy induced hypertension (2%) and thromboembolism (0.6%) were also observed. The abortion rate was 10.6%. There were 3 stillbirths (2%), another 6.7% babies were born preterm and 28% were lighter than appropriate for the period of gestation. There were no neonatal deaths. Coumarin derivatives were not associated with obvious foetal malformation.

Conclusion: With appropriate care, the outcome of pregnancy in women who have had cardiac surgery is favourable, if their functional class is good (JPMA 53:407;2003).

Introduction

Structural cardiac abnormalities predominate the spectrum of cardiac disease in the developed world.¹⁻³ In developing countries like Pakistan, rheumatic heart disease poses a challenge for cardiologists and cardiac surgeons.⁴⁻⁷ With improvement in prognosis following corrective cardiac

surgery, more women are being seen by obstetricians during pregnancies following cardiac surgery. As pregnancy in these, high risk group of women has an enormous impact on maternal and foetal outcome, a greater understanding of the disease and its management during pregnancy is required to adopt better counseling and treatment strategies.

Patients and Methods

A prospective study of 128 pregnant women with a history of cardiac surgery was undertaken between January 1990 and December 1999. Seven women were lost to follow up, and were therefore excluded from the study. Eight women who were pregnant but the outcome of pregnancy was not known till the end of the study period, were also excluded, leaving a total of 113 women. Data was collected about the women's age and parity, at the time of surgery. The details of the nature of the cardiac lesion and surgery were available in all cases and verification was also obtained from the Cardiac Institute, when found necessary. The details of previous pregnancies, if any and their outcome were recorded. The number of pregnancies before and after corrective surgery and any complications were noted. The women were under the joint care of obstetricians and cardiologists. The cardiac status was assessed functionally in accordance with New York Heart Association.⁸ Additional investigations including electrocardiography and echocardiography etc. were performed as and when indicated. An ultrasound examination at the initial visit for confirmation of pregnancy and its period of gestation, and another one at 18 to 20 weeks gestation for exclusion of foetal abnormality was done. All women with rheumatic heart disease continued to receive intramuscular injection Benzathene Penicillin G 1200 000 units every month throughout pregnancy.⁴ Those on anticoagulants were administered Injection Heparin 10,000 units subcutaneously twice a day, on confirmation of pregnancy, till 13 weeks gestation when they were prescribed Warfarin tablets. The coagulation profile was monitored by Prothrombin time (PT) and activated partial Prothrombin time (APPT) on alternate days, and the dose adjusted to keep the APTT two and a half times normal. Oral anticoagulants were stopped and Injection Heparin restarted at completion of 37 weeks, or earlier if delivery was anticipated. Heparin was withheld in labour and resumed 6 to 12 hours following delivery. Warfarin was recommenced 48 hours postpartum and Heparin was discontinued 12 hours following that. Other medication like Digoxin, beta blockers or diuretics were prescribed and the dose adjusted as advised by the cardiologists. Iron and folic acid supplements were prescribed for all.

Miscarriage was defined as foetal loss before 20 completed weeks of gestation. Premature delivery was considered a delivery between 20 and 37 weeks of gestation.

If the cardiac status allowed it, these women were given ambulatory care till 36 weeks of pregnancy. After this they were given the option of hospitalization. In the absence of an obstetric indication, spontaneous labour was awaited. During labour, they were kept propped up and given oxygen

by face mask as needed. If oxytocic stimulation was required, concentrated solutions were used to minimize intravenous fluid load. Six hourly intravenous injection of 500 mg. Ampicillin/Cephadrine alongwith 8 hourly injection of 80 mg. Gentamycin were given following amniotomy or spontaneous rupture of membranes.⁴ Injection Pentazocine 30mg alongwith Injection Promethazine 25 mg. was given intramuscular for analgesia, as required. The second stage of labour was shortened by applying outlet forceps or Ventouse after local perineal infiltration. If indicated, Pudendal block using 10-20 ml. Of 2% Lignocaine was also carried out. The third stage of labour was managed actively after intravenous administration of 10 units synthetic oxytocin at the time of delivery of the anterior shoulder. The baby was received by a Paediatrician. Its weight, Apgar score and detailed examination was recorded in the notes. All babies were given intramuscular injection of vitamin K, 1 mg. soon after delivery. Early breastfeeding and rooming in were encouraged. The mother continued to receive injectable antibiotics for 48 hours, which were then replaced by a broad spectrum oral preparation, Cap. Ampicillin/Cephadrine 500 mg. 6 hourly for another five days.

These women were advised to remain in hospital for at least five days after a vaginal delivery and seven days after a Caesarean Section. Barrier methods were advocated for birth spacing. If tubal ligation was requested for, it was performed by mini laparotomy under local anaesthesia at least six days following delivery, and patients were allowed home after another day.

General anaesthesia using Thiopentone, Halothane or Nitrous Oxide was administered when a surgical intervention was required.

Results

One hundred and seventy pregnancies in 113 women were reported, giving a mean pregnancy rate of 1.5 per woman. Of them 18 ended in spontaneous abortion, giving a rate of 0.16 per woman. Pregnancies were analysed separately in each diagnostic group and compared between groups. Valvular heart disease was the predominant lesion in 103 of 113 women (91.15%), with mitral valve being involved in 92 (89.32%). Table I shows the characteristics of all the pregnant women in different diagnostic groups.

Table 2 shows the outcome of these 170 pregnancies following cardiac surgery. A total of 150 (88.24%) went beyond 20 weeks gestation and vaginal delivery was possible in 132(88%). Caesarean section was required in 18 deliveries (12%). These included two elective procedures, one done because of two previous sections, and the other for a previous section with an inadequate pelvis.

Table 3 shows that repeat emergency cardiac surgery

Table 1. Profile of pregnant women with previous cardiac surgery (n=113).

	Valvular disease (n=103)						Repaired septal defect		Corrected TOF**	Repaired aortic aneurysm
	Mitral		Aortic		Pulmonary		Atrial	Ventricular		
	Valvotomy	Replacement	Valvotomy	Replacement	Valvotomy	Replacement				
	54	38	2	5*	1	3	1	4	4	1*
Age at surgery (yrs.)										
<20	8	6	-	-	-	1	-	1	4	-
21-25	28	7*	1	1*	-	1	-	2	-	1
26-30	16	22	1	2	-	1	1	1	-	-
>30	2	3	-	3	1	-	-	-	-	-
Pregnancies before Surgery (n=30)	15	6	2	-	3	-	-	1	1	2
Pregnancies after Surgery (n=160)	73	51	7	7	3	7	3	9	9	1

*One woman had mitral as well as pulmonary valve replacement.

**Tetralogy of fallot

Table 2. Pregnancy outcome and mode of delivery after cardiac surgery (n=170).

	Valvular disease (n=103)						Repaired septal defect		Corrected TOF	Repaired aortic aneurysm
	Mitral		Aortic		Pulmonary		Atrial	Ventricular		
	Valvotomy	Replacement	Valvotomy	Replacement	Valvotomy	Replacement				
Abortion (n=18)	4	8	-	2	-	1	1	1	1	-
Tubal pregnancy (Laparotomy n=2)	-	1	-	-	-	-	-	1	-	
Vag. Delivery (n=132)										
SVD	14	2	1	2	-	-	1	1	-	-
Outlet forceps	47	30	2	2	1	4	-	1	4	-
Ventouse	6	1	-	-	-	-	-	2	2	-
Assisted breech	4	1	2	-	-	1	-	-	1	-
Caesarean section (n=18)	4	7	2	1	-	1	-	1	1	1

Table 3. Maternal complications in pregnancy following cardiac surgery (n=170).

	Valvular disease (n=103)						Repaired septal defect		Corrected TOF	Repaired aortic aneurysm
	Mitral		Aortic		Pulmonary		Atrial	Ventricular		
	Valvotomy	Replacement	Valvotomy	Replacement	Valvotomy	Replacement				
Repeat surgery in pregnancy										
- Repeat valvotomy	1	-	-	-	-	-	-	-	-	-
- Repeat replacement with C/Section	-	1	-	-	-	-	-	-	-	-
During peurperium	-	1	-	-	-	-	-	-	-	-
Epistaxis	-	2	-	-	-	1	-	-	-	-
Haematoma at episiotomy site	-	1	-	-	-	1	-	-	-	-
Thromboembolism (hemiplegia)	1	-	-	-	-	-	-	-	-	-
Abruptio placentae	1	1	-	1	-	-	-	1	-	-
Pulmonary oedema	16	8	1	1	-	-	-	-	1	-
Postpartum haemorrhage	3	2	-	-	-	1	-	-	-	-
Pre-eclampsia	-	-	1	1*	-	1	-	-	1	1*
Arrythmias	3	2	-	-	1	-	-	-	1	1*

Table 4. Foetal outcome after 20 weeks in pregnancy following cardiac surgery.

	Valvular disease						Repaired septal defect		Corrected TOF	Repaired aortic aneurysm
	Mitral		Aortic		Pulmonary		Atrial	Ventricular		
	Valvotomy	Replacement	Valvotomy	Replacement	Valvotomy	Replacement				
Still birth (3)	-	2	-	1	-	-	-	-	-	-
Preterm delivery (10)	3	2	1	-	1	-	1	-	2	-
Small for dates (42)	22	13	1	-	1	-	2	1	1	1

pregnancy. She went into spontaneous labour following this and delivered a live baby by outlet forceps. Her condition improved on conservative measures and the valvular function was not compromised on follow up. There was no case of infective endocarditis or maternal death.

The foetal outcome is shown in Table 4. There were three stillbirths (2%). These women were on Warfarin at the time the intrauterine death was confirmed, in two of these cases there was placental abruption but without evidence of coagulopathy. There was no apparent congenital malformation in these stillborn babies. Autopsies were requested to determine the exact cause of foetal demise, but were not allowed by the family. There was no intrapartum foetal loss. Ten infants delivered preterm (6.67%). In two of these cases, delivery was undertaken in view of deteriorating maternal condition due to severe pregnancy induced hypertension. Forty two (28%) infants were lighter than appropriate for the period of gestation. There was no obvious foetal abnormality or intracranial haemorrhage. No death was reported in the neonatal period.

Discussion

Despite improvements in cardiac surgery and subsequent prognosis, pregnancy in these women requires vigilant care. The haemodynamic changes of pregnancy put additional circulatory burden on the heart, which is maximum during labour and immediately following delivery.^{4,9,10}

In Pakistan, most of the women in childbearing age who have cardiac surgery, suffer from rheumatic heart disease, and therefore mitral valve commissurotomy or replacement are the commonest procedures carried out in them. The majority of women had surgery between 20 and 30 years of age, this indicates the severity of their symptoms preoperatively. Still it is possible for valvular heart disease to be undetected when the woman is pregnant.⁴ Even then these symptoms may be attributed to physiological changes of pregnancy. This occurred in six previous pregnancies, when the symptoms were thought to be related to pregnancy by care givers. In these cases, the diagnosis had first been made by cardiologists in early puerperium, when symptoms had worsened instead of improving. The same is evident when one looks at the number of pregnancies before and after surgery. Marriage, child bearing and rearing are considered essential components of a woman's life in Pakistan. Those with mitral valve disease that required valve replacement, presumably had severer disease and symptoms. In this group of women, there were only six pregnancies prior to and 50 after surgery. In comparison there were 15 pregnancies preoperatively and 69 after surgery in women who required mitral commissurotomy. In these women, perhaps the symptoms were less of a deterrent and surgery was

deferred by patients and their families till after marriage and childbearing.

The functional status of the woman in the prepregnancy state is considered a better predictor of maternal and foetal outcome as compared to the type of lesion requiring surgery.^{4, 12,13} This was true for patients in this series also. However it is worth noting that patients who had surgery for correction of congenital defects like isolated septal defects, tetralogy of Fallot or cardiac manifestations of Marfan's syndrome, had relatively few problems. This is in accordance with similar finding from others.¹⁴

Valve replacement was performed using mechanical prostheses which, as compared to bioprosthetic valves, have a lower risk of deterioration in function due to additional burden of pregnancy.^{15,16} Pregnancy being a hypercoagulable state, has an increased risk of thromboembolism and thrombosis of prostheses, therefore anticoagulant therapy is indicated in these women.^{12,17} Administration of heparin in the first trimester, oral coumarins thereafter till term, and Heparin again till after delivery, has the advantage of minimizing the teratogenic effects of Coumarins in period of organogenesis, particularly between 6 to 12 weeks.^{18,19} Coumarins in the second trimester are advocated because of the ease of their administration, avoiding non compliance. Substitution with Heparin once again before labour is a precaution against postpartum haemorrhage, and foetal or neonatal complications like neurologic sequelae due to intraventricular haemorrhage. Alternative regimes are food for thought but their effectiveness and complications, apart from limited clinical experience, make them less acceptable.^{16,20-26}

The abortion rate was 10.5%, which is comparable to the general population.^{27,28} Vaginal delivery was possible in 88%. This corroborates that increasing rates of Caesarean section do not imply better care, and should be reserved primarily for obstetric indications. The cardiac patient who can tolerate Caesarean section is likely to tolerate labour and vaginal delivery just as well.^{29,30}

If unavoidable, commissurotomy during pregnancy is well accepted and has relatively few maternal and foetal risks.³¹⁻³³ Recently percutaneous mitral valve commissurotomy has been recommended as the procedure of choice in pregnancy.³⁴⁻⁴⁰ Some women perceive the risk to be over with the end of pregnancy, or tend to neglect themselves with the additional responsibility of looking after a newborn baby. The patient who required a mitral valve replacement of a thrombosed prosthesis on the 13th postnatal day, had stopped anticoagulant therapy on being allowed home 7 days earlier. This underscores the significance of appropriate counseling after delivery.

Anticoagulant therapy can also predispose to haem-

Anticoagulant therapy can also predispose to haemorrhage.^{12,13} Problems like haematoma at the episiotomy site can be minimized by attention to suturing technique and haemostasis, in addition to good control of coagulation status.

Pulmonary oedema can be an extremely distressing life threatening emergency. Of those who it occurred in, almost all had mitral valve valvotomy. Except for the three cases that required emergency repeat cardiac surgery, the condition responded to conservative measures, diuretics, digitalization and beta blockers. Beta blockers are effective recommended agents for controlling tachycardia and pulmonary oedema in pregnancy.^{41,42} The risk of associated foetal bradycardia and growth restriction is not significant with minimal exposure in the latter half of pregnancy.⁴³

Cardiac arrhythmias were a cause of concern, due to their increased association with thromboembolism and death.⁴¹ Fortunately, the one patient who had thromboembolism, responded favourably to conservative measures. The prevalence of pre eclampsia in this series is not more than others^{30,45,46}, or the general population.

Twenty eight percent newborns in this series were lighter than appropriate for the period of gestation. This does not compare unfavourably with the incidence of low birth weight in the general population of Pakistan or the region.⁴⁷⁻⁴⁹ Although abruptio placentae occurred in women on Coumarins, but cannot be attributed solely to anticoagulants because their haematological profiles were all well controlled. All neonates had a detailed clinical assessment including that for congenital anomalies. It is worth remembering that absence of an apparent congenital abnormality in the newborns does not completely exclude these. The stillborn babies too, were apparently normal but the parents did not consent to autopsy. Echocardiography of the newborns was not carried out for congenital cardiac malformations. This is recommended especially when the mothers have a congenital cardiac lesion.^{50,51} Haematological complications were not observed in any newborn.

Concerns remain about the outcome of pregnancy in this high risk group of women.^{52,53} There is however some encouraging news. In conformity with similar findings from other centers⁵⁴, it is observed that if the functional class is favourable and the care administered during pregnancy and confinement is of the recommended standards, these women can be reassured.

References

- McFaul PB, Dornan JC, Lamki H, et al. Pregnancy complicated by maternal heart disease: a review of 519 women. *Br J Obstet Gynaecol* 1998;95:861-7.
- Land MA, Bisno AL. Acute Rheumatic fever-a vanishing disease in suburbia. *JAMA* 1983;249:895.
- Szekely P, Turner R, Smith L. Pregnancy and the changing pattern of rheumatic heart disease. *Br Heart J* 1973;35:1293-1303.
- Teerlink JR, Foster J. Valvular heart disease in pregnancy: a contemporary perspective. *Cardiol Clin* 1998;16:573-98.
- Visser AA, Coetzee EJ, Grobler CJF, et al. Cardiac disease. In: Cronje HS, Grobler CJF, Visser AA (eds). *Obstetrics in Southern Africa*. Pretoria: JL van Schaik. 1996, p. 226.
- Bull World Health Org 1992;70:213-18.
- Sadiq M, Nazir M, Sheikh SA. Infective endocarditis in children-incidence, pattern, diagnosis and management in a developing country. *Int J Cardiol* 2001;78:175-82.
- New York Heart Association Criteria Committee, 1964. Nomenclature and criteria of diagnosis of diseases of the heart and great vessels. 8th edition: Bosta: Little Brown, 1979, p. 51.
- Elkayam U. Pregnancy and cardiovascular disease. In: Braunwald E (ed). *Heart Disease: a textbook of cardiovascular medicine* (eds). Philadelphia: Saunders, 1997, pp. 1843-64.
- Gilson GJ, Samaan S, Crawford MH, et al. Changes in haemodynamics, ventricular remodelling and ventricular contractility during normal pregnancy: a longitudinal study. *Obstet Gynaecol* 1997; 89:957-62.
- Ueland K, Hanson JM. Maternal cardiovascular dynamics: labour and delivery under local and caudal analgesia. *Am J Obstet Gynaecol* 1969;103: 8-18.
- Suri V, Sawhney H, Vasishta K, et al. Pregnancy following cardiac valve replacement surgery. *Int J Gynecol Obstet* 1999;64:239-46.
- Lecuro F, Desnos M, Taurelle R. Anticoagulant therapy in pregnancy. *Acta Obstet Gynecol Scand* 1996;5:217-26.
- Siu SC, Sermer M, Harrison DA, et al. Risk and predictors for pregnancy related complications in women with heart disease. *Circulation* 1997;96:2789-94.
- Lee CN, Wu CC, Lin PY, et al. Pregnancy following cardiac prosthetic valve replacement. *Obstet Gynaecol* 1994;83:353-6.
- Sbarouni E, Oaklay CM. Outcome of pregnancy in women with valve prosthesis. *Br Heart J* 1994;71:196-201.
- Stein PD, Alpert JS, Copeland J, et al. Antithrombotic therapy in patients with mechanical and bioprosthetic heart valves. *Chest* 1995;108(Supp):371S-9S.
- Hall JG, Pauli RM, Wilson KM. Maternal and foetal sequelae of anticoagulation during pregnancy. *Am J Med* 1980;68:122-40.
- Iturbe-Alessio I, Fonseca MC, Mutchinik O, et al. Risks of anticoagulant therapy in pregnant women with artificial heart valves. *N Eng J Med* 1986;315:1390-3.
- Ginsberg JS, Hirsh J. Use of antithrombotic agents during pregnancy. *Chest* 1995;108(Supp):S305-S11.
- Kumar P, Venugopal P, Kaul U, et al. Pregnancy in patients with prosthetic cardiac valve: a ten year experience. *Scand J Thorac Cardiovasc Surg* 1998;22:19-22.
- Weitz JI. Low molecular weight heparins. *N Engl J Med* 1997;337:688-98.
- Lee LH, Liauw PC, Ng AS. Low molecular weight heparin for thromboprophylaxis during pregnancy in 2 patients with mechanical mitral valve replacement. *Thromb Haemost* 1996;76:628-30.
- Sorensen HT, Johnsen SP, Larsen H. Birth outcomes in pregnant women treated with low-molecular-weight heparin. *Acta Obstet Gynaecol Scand* 2000;79: 655-9.
- Salazaar E, Izaguirre R, Verdejo J, et al. Failure of adjusted doses of heparin to prevent thromboembolic phenomenon in pregnant patients with mechanical cardiac valve prostheses. *J Am Coll Cardiol* 1996;27:1698-1703.
- Blickstein D, Blickstein I. The risk of foetal loss associated with warfarin anticoagulants. *Int J Gynaecol Obstet* 2002;78:221-5.
- Risch HA, Weiss NS, Clarke EA, et al. Risk factors for spontaneous abortions and its recurrence. *Am J Epidemiol* 1990;131:570-3.
- Garcia-Enguidanos A, Calle ME, Valera J, et al. Risk factors in miscarriage: a review. *Eur J Obstet Gynecol Reprod Biol* 2002;102:111-19.
- Robson SC, Hunter S, Moore M, et al. Haemodynamic changes during the puerperium: a doppler and M mode echocardiographic study. *Br J Obstet Gynaecol* 1987;94:1028-39.
- Desai DK, Adan LM, Naidoo DP, et al. Mitral stenosis in pregnancy: a four year experience at King Edward VIII Hospital, Durban. *South Africa Br J Obstet Gynecol* 2000;107:953-8.
- de Sweit M, Deverall P. Pregnancy-still an indication for closed mitral valvo-

31. de Sweit M, Deverall P. Pregnancy-still an indication for closed mitral valvotomy. *Int J Cardiol* 1990;26:323-4.
32. Stephen SJ. Changing patterns of mitral stenosis in childhood and pregnancy in Sri Lanka. *J Am Coll Cardio*. 1992;19:1276-84.
33. Carabello BA. Timing of surgery in mitral and aortic stenosis. Valvular heart disease. *Cardio Clin* 1991;9:229-35.
34. Patel JJ, Mitha AS, Hassen F, et al. Percutaneous balloon mitral valvotomy in pregnant patients with tight pliable mitral stenosis. *Am Heart J* 1993;125:1106-9.
35. Kalra GS, Arora R, Khan JA, et al. Percutaneous mitral commissurotomy for severe mitral stenosis during pregnancy. *Cathet Cardiovasc Diagn* 1994;33:28-31.
36. Dommissie J, Commerford PJ, Levettan B. Balloon valvoplasty for severe mitral stenosis in pregnancy. *S Afr Med J* 1996;86:1194-6.
37. Ben Farhat M, Gamra H, Betbont F, et al. Percutaneous balloon mitral valvotomy during pregnancy. *Heart* 1997;77:567-70.
38. Iung B, Cormier B, Elias J, et al. Usefulness of percutaneous balloon commissurotomy for mitral stenosis during pregnancy. *Am J Cardiol* 1994;73:398-400.
39. Goldstein SA, Campbell AN. Mitral stenosis: evaluation and guidance of valvoplasty by transoesophageal echocardiography. *Cardiol Clin* 1993;11:409-25.
40. Saleh MA, El Fiky AA, Fahmy M, et al. Use of biplane transoesophageal echocardiography as the only imaging technique for percutaneous balloon mitral commissurotomy. *Am J Cardiol* 1996;78:103-6.
41. Avila WS, Grinberg M, Decount LV, et al. Clinical course of women with mitral valve stenosis during pregnancy and puerperium. *Arq Bras Cardiol* 1992;58:359-64.
42. Narasimhan C, Joseph G, Thomas CS. Propranolol for pulmonary oedema in mitral stenosis. *Int J Cardiol* 1994;44:178-79.
43. Butlers L, Kennedy S, Rubin PC. Atenolol in essential hypertension during pregnancy. *BMJ* 1990;301:587-9.
44. Szekely P, Snaith L. Obstetric care and the fetus in rheumatic heart disease. In: Szekely P, Snaith L (eds). *Heart disease and pregnancy*. Edinburgh: Churchill Livingstone 1974, p. 137.
45. Zuber M, Gautschi N, Oechslin E, et al. Outcome of pregnancy in women with congenital shunt lesions. *Heart* 1999;81:271-5.
46. Moodley J. Pre-eclampsia/eclampsia syndrome. *S Afr J Cont Med Educ* 1997;15: 31-41.
47. Fikree F, Azam SI, Berendes HW. Time to focus child survival programmes on the newborn: assessment of levels and causes of infant mortality in rural Pakistan. *Bull WHO* 2002;80:271-6.
48. Najmi RS. Distribution of birth weights of hospital born Pakistani infants. *J Pak Med Assoc* 2000;50:121-4.
49. Mondal B. Low birthweight in relation to sex of baby, maternal age and parity: a hospital based study on Tangsa tribe from Arunachal Pradesh. *J Med Assoc* 1998; 96:362-4.
50. Bitsch M, Johansen C, Wennevold A, et al. Pregnancy in women with congenital heart disease. *Ugesk Laeger* 1989;151:2574-6.
51. Whittemore R, Wells TA, Castellsague X. A second generation study of 427 probands with congenital heart defects and their 837 children. *J Am Coll Cardiol* 1994;23:1459-67.
52. Ayhan A, Yucel A, Bildici I, et al. Feto-maternal morbidity and mortality after cardiac valve replacement. *Acta Obstet Gynecol Scand* 2001;80:713-18.
53. Siu SC, Colman JM, Sorensen S, et al. Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease. *Circulation* 2002;105:2179-84.
54. Mane SV, Gharpure VP, Merchant RH. Maternal Heart disease and perinatal outcome. *Indian Pediatr* 1993;30:1407-11.