

RESEARCH ARTICLE

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Midterm results after arterial switch operation for transposition of the great arteries: a single centre experience

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Abstract

Background: The arterial switch operation (ASO) has become the surgical approach of choice for d-transposition of the great arteries (d-TGA). There is, however an increased incidence of midterm and longterm adverse sequelae in some survivors. In order to evaluate operative risk and midterm outcome in this population, we reviewed patients who underwent ASO for TGA at our centre.

Methods: In this retrospective study 52 consecutive patients with TGA who underwent ASO between 04/1991 and 12/1999 were included. To analyze the predictors for mortality and adverse events (coronary stenoses, distortion of the pulmonary arteries, dilatation of the neo-aortic root, and aortic regurgitation), a multivariate analysis was performed. The follow-up time was ranged from 1–10 years (mean 5 years, cumulative 260 patient-years).

Results: All over mortality rate was 15.4% and was only observed in the early postoperative period till 1994. The predictors for poor operative survival were low APGAR-score, older age at surgery, and necessity of associated surgical procedures. Late re-operations were necessary in 6 patients (13.6%) and included a pulmonary artery patch enlargement due to supravalvular stenosis (n = 3), coronary revascularisation due to coronary stenosis in a coronary anatomy type E, aortic valve replacement due to neo-aortic valve regurgitation (n = 2), and patch-plasty of a pulmonary vein due to obstruction (n = 1). The dilatation of neo-aortic root was not observed in the follow up.

Conclusions: ASO remains the procedure of choice for TGA with acceptable early and late outcome in terms of overall survival and freedom of reoperation. Although ASO is often complex and may be associated with morbidity, most patients survived without major complications even in a small centre.

Keywords: Arterial switch operation, Transposition of great arteries, Midterm outcome

Background

Since the introduction of the arterial switch operation (ASO) by Jatene et al. in 1975 [1], the procedure has become the surgical treatment of choice for the anatomical repair of the transposition of the great arteries (TGA). A limited number of long-term studies revealed an excellent survival and freedom from re-operation in patients

undergoing ASO [2-6]. However, one of the major concerns about the ASO is the possible deterioration of neo-aortic valve function with a dilatation of neo-aortic root [7] and the stenoses of coronary arteries which appear occasionally and needs surgical intervention [2]. The purpose of the present study was to review our results of ASO for TGA and to evaluate early and midterm survival rates, morbidity, and complications in a single centre cohort retrospectively followed up for as long 10 years. Moreover, risk factors for mortality and adverse midterm events after ASO for TGA (coronary stenoses, distortion of the pulmonary arteries, dilatation of the neo-aortic root, and aortic valve regurgitation) were the endpoints of interest.

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Methods

Study population

The retrospective single centre study was approved by the ethics committee of the Medical Faculty, University of Göttingen. Between April 1991 and December 1999, 52 consecutive patients (median age 10 ± 49 days, range 2–338 days) underwent an ASO at the University of Göttingen.

Data collection

All perioperative data was collected retrospectively with the help of medical records, echocardiographic and cardiac catheterization data as well operative notes. The clinical follow-up included an examination by the referring pediatric cardiologist at regular intervals or in our institution by the pediatric cardiologist. The echocardiographic data for the study was taken from the cardiologists' report. The midterm follow-up was obtained by review of patient records and clinic notes.

Patients' characteristics

For 52 patients, including 37 males and 15 females, the median age at time of surgery was 10 ± 49.61 days (range, 2–338 days). The initial diagnosis was a simple TGA in 34 (66%) patients, TGA with a ventricular septal defect (VSD) in 10 (19%) patients, Taussig-Bing in 2 (4%) patients, TGA with coarctation of the aorta (CoA) in 2 (4%) patients, and TGA with CoA and VSD in 4 (8%) patients. 42 patients received Rashkind's balloon atrial septostomy and the duration between septostomy to surgery was 7 ± 42.45 days (range, 1–271 days).

Standard surgical techniques were used. The following details were considered. A single initial infusion of crystalloid (Brettschneider solution) cardioplegia was used for the majority of the series with a dose of 30 ml/kg over 7 minutes. In five cases a total circulatory arrest with deep hypothermia (18°C) was necessary for CoA repair.

Prior to ASO, 8 patients had cardiac surgical procedures which were Blalock-Hanlon Operation ($n = 3$), pulmonary artery banding ($n = 2$), CoA correction ($n = 2$), and CoA correction with an aortic arch obstruction repair ($n = 1$). We had 3 preterm births. One was with 31 completed weeks and with bronchopulmonary dysplasia. The second was with 35 completed weeks, and the remaining one had 36 completed weeks and had a respiratory distress syndrome and a diabetic fetopathy.

A total of 34 patients (66%) were mechanically ventilated and 3 patients had a complication (intracranial hemorrhage, renal dysfunction, chest infection) before ASO. On echocardiographic examination a mean diameters of the aorta and the pulmonary artery were 11 ± 1.56 mm (range, 8–15 mm) and 12 ± 1.84 mm (range, 10–17 mm) respectively. Preoperative catheterization was

performed in all patients and coronary pattern was identified with aortography or coronary angiography. It was in the beginning a standard protocol. Currently, we changed that protocol. Not every patient received a catheterization preoperative nowadays. Moreover, it was also a part of the protocol in our department to leave the chest open some cases to aid in hemodynamic and respiratory stability in the initial postoperative period.

In accordance with the Yacoub's coronary classification [8], 45 patients were encountered for type A, 3 for type B, and another 3 for type E. One case that did not precisely fit into one of the described categories was classified as Type B1 according the Sauer classification [9]. The preoperative characteristics of the patients at the time of ASO are shown in Table 1.

Statistics analysis

Statistical analysis was performed by using commercial statistic software (Statistica 5.1.[®], StatSoft Inc., Tulsa, OK, USA). Descriptive data for continuous variables are presented as mean \pm SD, and categorical variables are presented as relative frequencies. A multivariate analysis was performed by means of a logistic regression model for the endpoint of in-hospital mortality and by means of a Cox proportional hazard model for the endpoints of late mortality. Variables with P values less than 0.05 in univariate analysis were entered into the multivariate models. Freedom from time-related events was calculated using the product-limit method of Kaplan-Meier.

Results

Intraoperative characteristics

A standard ASO was performed in all patients, including a *Lecompte maneuver*. The techniques for the coronary artery transfer varied depending on the coronary anatomy and included the *trap door technique*.

Surgery was performed in moderate hypothermia (24°C). Myocardial protection was achieved by application of Bretschneider's crystalloid cardioplegia (Custidiol HTK, Köhler Chemie, Germany). The right atrium was then incised and the cardioplegic solution was aspirated from coronary sinus. After transection of the great vessels, the coronary arteries were excised (in U fashion) and subsequently re-implanted in the neo-aorta. The Lecompte maneuver was performed before anastomosis of the neo-aortic root and distal ascending aorta was completed. The neo-pulmonary trunk was reconstructed with pantaloony-like untreated autologous pericardial patch. Then, the atrial septal defect (or a large foramen ovale) was closed, usually by running suture. Finally, the anastomosis between the distal pulmonary artery and the neo-pulmonary trunk was performed. Reperfusion of the heart and re-warming started after closure of the atrial septal defect.

Table 1 Preoperative characteristics

| | Patients or Mean | % or Range |
|---|------------------|--------------|
| Age at correction (d) | 10 ± 49.61 | 2-338 |
| Female/Male | 15/37 | |
| Weight (g) | 3505 ± 575.04 | 2480-5420 |
| Body surface area (qm) | 0.22 ± 0.03 | 0.13-0.18 |
| TGA pathology | | |
| Simple TGA | 34 | 65.4 |
| TGA with VSD | 10 | 19.3 |
| Taussig-Bing | 2 | 3.8 |
| TGA with CoA | 2 | 3.8 |
| TGA with CoA + VSD | 4 | 7.6 |
| Preoperative cardiopulmonary support | | |
| Prostaglandin therapy | 42 | 80.8 |
| Duration between Rashkind maneuver to surgery | 7 ± 42.45 | 1-271 |
| Balloon atrial septostomy | 48 | 92.3 |
| Surgery prior Switch | | |
| Blalock-Hanlon-Operation | 3 | 5.7 |
| Pulmonary artery banding | 2 | 3.8 |
| CoA correction | 2 | 3.8 |
| CoA correction and AAO repair | 1 | 1.9 |
| Complications prior surgery | | |
| Intracranial hemorrhage | 1 | 3.8 |
| Renal disorder | 1 | 3.8 |
| Chest infection | 1 | 3.8 |
| Mechanical ventilatory support | 34 | 65.4 |
| Vital parameter prior surgery | | |
| Mean arterial pressure (mmHg) | 59 ± 10.49 | 37-85 |
| Heart rate (beats/min) | 140 ± 16.98 | 110-183 |
| Dimensions of great vessels | | |
| Mean diameter of the aorta (mm) | 11 ± 1.56 | 8-15 |
| Mean diameter of pulmonary artery (mm) | 12 ± 1.84 | 10-17 |
| Coronary pattern (Yacoub) | | |
| A/D/E | 45/3/3 | 86.5/5.8/5.8 |
| Coronary pattern (Sauer) | | |
| B1 | 1 | 1.9 |

TGA: Transposition of the great arteries; VSD: ventricular septal defect; CoA: Coarctation of the aorta;
 AAO: aortic arch obstruction.

Along with the ASO, 22 concomitant procedures were performed including closure of VSD (n = 15), closure of VSD with repair of CoA (n = 3), re-repair of CoA (n = 2), and pulmonary artery de-banding (n = 2). The mean cardiopulmonary bypass (CPB) time and the mean aortic cross clamp time was 231.5 ± 96.16 minutes (range, 129–838 minutes) and 94 ± 26.18 minutes (range, 58–152 minutes) respectively. The mean body core temperature was 24.5 ± 2.54°C (range, 17–27.5°C). In 34 (66%) patients the

chest was left open for a delayed sternal closure. There were 2 (4%) intraoperative deaths which occurred during 1991–1994. All the results are summarized in Table 2.

Postoperative characteristics

The postoperative characteristics of patients are shown in Table 3. Within the first 24 hours the left arterial pressure (LAP) was 12 ± 3.88 mmHg (range, 5–21 mmHg) and the mean arterial pressure was 54 ± 7 mmHg (range,

Table 2 Intraoperative characteristics

| | Patients or Mean | % or Range |
|-------------------------------|------------------|------------|
| Additional procedures | 22 | 42.3 |
| VSD closure | 15 | 28.8 |
| VSD closure and CoA | 3 | 5.8 |
| CoA re-repair | 2 | 3.8 |
| Debanding of pulmonary artery | 2 | 3.8 |
| Duration of surgery (min) | 414 ± 106.56 | 220-865 |
| Intraoperative | | |
| CPB (min) | 231.5 ± 96.16 | 129-838 |
| Ischemic time (min) | 94 ± 26.18 | 58-152 |
| Core temperature (C°) | 24.5 ± 2.54 | 17-27.5 |
| Nitroprusside (µg/kg/min) | 0.6 ± 0.67 | 0.1-3 |
| Open chest after surgery | 34 | 65.4 |
| Death | 2 | 3.8 |

VSD: ventricular septal defect; CoA: Coarctation of the aorta, CPB: Cardiopulmonary bypass.

41–70 mmHg). The Levels of serum creatine phosphokinase (S-CPK) and serum creatine phosphokinase-MB (CPK-MB) were 41 ± 307 U/L (range, 41–1463 U/L) and 25.5 ± 21 U/L (range, 7–85 U/L) respectively. In intensive care unit (ICU) the transfusion of red cell and fresh frozen plasma was calculated to 294 ± 163 ml (range, 75–686 ml) and 330 ± 363 ml (range, 50–1310 ml) respectively. The duration of postoperative mechanical ventilation was 6 ± 6 days, (range, 1–28 days) and 11 (25%) patients required re-intubated due to respiratory failure. The mean ICU length of stay was 10 ± 10.83 days (range, 5–57 days), and the mean hospital stay was 26 ± 16.33 days (range, 14–98 days).

Early complication occurred in 4 patients. In 1 (2%) a pacemaker was implanted due to complete AV block, 1 (2%) had a myocardial infarction, and 1 (2%) had two rethoracotomies. This patient had a surgical bleeding on the first postoperative day which was successfully treated and on the 22nd postoperative day right atrial thrombi were detected on echocardiography, presumably due to a central venous catheter, which required surgical removal.

The postoperative echocardiography at time of discharge was performed in all patients and is summarized in Table 3. The peak velocity (Vmax) in the pulmonary artery and the aorta were 1.9 ± 0.63 m/s (range, 0.9-3.2 m/s) and 1.5 ± 0.29 m/s (range, 1.2-2.9 m/s) respectively (data diameters of the neo-aortic root indexed to BSA were not available). The fractional shortening of the left ventricle was normal in all patients (35% ± 7%; range, 22% to 46%). The measurements of LV end-diastolic and end-systolic diameters were 21 ± 2.3 mm (range, 17 to 26 mm) and 14 ± 3 mm (range, 8 to 20 mm) respectively which were within normal range.

Table 3 Postoperative characteristics

| | Patients or Mean | % or Range |
|--|------------------|------------|
| First 24 hrs | | |
| LAP (mmHg) | 12 ± 3.88 | 5-21 |
| Mean arterial pressure (mmHg) | 54 ± 7 | 41-70 |
| S-CPK (U/L) | 41 ± 307 | 41-1463 |
| S-CPK-MB (U/L) | 25.5 ± 21 | 7-85 |
| ICU | | |
| Red cell transfusion (ml) | 294 ± 163 | 75-686 |
| Fresh frozen plasma transfusion (ml) | 330 ± 363 | 50-1310 |
| Duration of mechanical ventilation (d) | 6 ± 6 | 1-28 |
| Re-intubation | 11 | 25 |
| Length of ICU stay (d) | 10 ± 10.83 | 5-57 |
| Length of hospital stay (d) | 25.5 ± 16.33 | 14-98 |
| Early complications | | |
| Pacemaker implantation | 1 | 2 |
| Myocardial infarction | 1 | 2 |
| Rethoracotomy | 1 | 2 |
| Echocardiography at discharge | | |
| Vmax pulmonary artery (m/s) | 1.9 ± 0.63 | 0.9-3.2 |
| Vmax aorta ascendens (m/s) | 1.5 ± 0.29 | 1.2-2.9 |
| LVEDD (mm) | 21 ± 2.3 | 17-25.7 |
| LVESD (mm) | 14 ± 3 | 8-20 |
| FS (%) | 35 ± 7 | 22-46 |

LAP: left atrial pressure; S-CPK: serum creatine phosphokinase; S-CPK-MB: creatine.

Phosphokinase-MB; ICU: Intensive care unit; Vmax: peak velocity; LVEDD: left ventricular end diastolic dimension; LVESD: left ventricular end-systolic dimension; FS: Fractional shortening.

Outcome

All over (1991–1999) mortality rate was 15.4% (n = 8) and was observed in the early postoperative period only till 1994. Out of these patients the majority (87.5%) died in the first 30 days after ASO.

Five patients died within first 24 hours postoperatively. In two of them weaning from CPB was failed due to irreversible left heart failure and one patient had an acute refractory right heart failure due to suspected malperfusion of the right coronary artery. This patient had a type E coronary pattern according Yacoub's classification. The remaining 2 patients underwent an uncomplicated surgery but died in ICU due to refractory left heart failure.

Two deaths occurred on second and fifth postoperative day on ICU due to multi organ failure related to a left heart failure. The last patient died on the 50th postoperative day due to poor hemodynamic conditions, multiple resuscitations and the cause of death was left heart failure. That patient did not receive a control angiography, because there was so far no indication for that. The initial course went uneventful. There were no signs of myocardial infarction and

the lab values did not show a myocardial ischemia. ECG and echocardiography were fine till day 20 postoperatively. Then the patient deteriorated with signs of left heart failure, which resulted in a multiorgan failure (Table 4). None of our patients received a revision of the coronary arteries in the early postoperative phase.

Late complications were observed in 7 patients and included convulsions in 1, myocardial malperfusion in 1, arrhythmia in 2, sternal wound infection in 1, and in 2 patients a chylothorax was observed.

The survivors were seen by the referring pediatric cardiologist at regular intervals or in our institution by the pediatric cardiologist. The follow-up time ranged from 1–10 years (mean 5 years, cumulative 260 patient-years) postoperatively. In majority of patients (93%), functional NYHA class I, with normal LV-function with no symptoms referable to the cardiovascular system was seen. There were no late deaths. Late re-operations were necessary in 9 (20%) patients and included a pulmonary artery patch enlargement due to supravalvular stenosis (n = 3), coronary revascularisation due to coronary stenosis in a coronary anatomy type E and aortic valve replacement due to neo-aortic valve regurgitation (n = 2), and patch plasty of a pulmonary vein due to obstruction (n = 1). Two patients required pacemaker implantation due to complete AV block and one patient due to sick sinus syndrome. The dilatation of neo-aortic root was not observed in any of the patients during the follow up (Table 5).

Risk factors for mortality

A linear regression analysis was performed to determine possible associations of anatomic and physiologic parameters with the mortality. The predictors' analysis for poor operative survival was: preterm birth (p = 0.0008), long duration between cardiac catheterization and surgery (p = 0.006), older age at surgery (p = 0.004), necessity of associated procedures (p = 0.004), redo surgery

Table 5 Outcome

| | Patients | % |
|---|----------|------|
| Mortality all over (1991–1999) | 8 | 15.4 |
| Late complications | | |
| Convulsions | 1 | 2.2 |
| Myocardial malperfusion | 1 | 2.2 |
| Arrhythmia | 2 | 4.4 |
| Sternal wound infection | 1 | 2.2 |
| Chylothorax | 2 | 4.4 |
| Follow up n = 44 | | |
| NYHA I | 41 | 93.2 |
| NYHA II | 0 | |
| NYHA III | 3 | 6.8 |
| NYHA IV | 0 | |
| Mortality | 0 | |
| Reoperations | | |
| Dilatation of neo-aortic root | 0 | |
| Pulmonary artery patch enlargement | 3 | 6.6 |
| Coronary revascularisation and aortic valve replacement | 2 | 4.4 |
| Patch plasty of a pulmonary vein | 1 | 2.2 |
| Pacemaker implantation | 3 | 6.6 |

NYHA: New York Heart Association.

(p = 0.04), prolonged ischemia (p = 0.0002), and no treatment with prostaglandin prior surgery (p = 0.002) (Table 6).

Discussion

The goal of this study was to identify predictors for mortality and to review adverse events after ASO for TGA (coronary stenoses, distortion of the pulmonary arteries, dilatation of the neo-aortic root, and aortic regurgitation). This study confirms that ASO can be performed with acceptable early and late outcome in patients with TGA even in a small centre after a learning process and modifications of the perioperative setting.

Table 4 Deaths

| No. | Age at surgery (d) | Accompanied diagnosis | Concomitant procedure | Cause |
|-----|---------------------|---|---|---|
| 1 | 16 | VSD | VSD closure | Right heart failure |
| 2 | 41 | VSD, CoA | VSD closure, CoA repair | Left heart failure |
| 3 | 5 | VSD | VSD closure | Left heart failure |
| 4 | 20 | VSD, CoA | VSD closure, CoA repair | Left heart failure |
| 5 | 144 | Taussig-Bing | - | Left heart failure |
| 6 | 338 [preterm, 31 w] | Taussig-Bing, bronchopulmonary dysplasia | Neo-aortic root enlargement with a pulmonary artery patch | Left heart failure, Multi organ failure |
| 7 | 7 [preterm, 36 w] | - | - | Left heart failure |
| 8 | 18 [preterm, 35 w] | respiratory distress syndrome, diabetic fetopathy | - | Left heart failure, Multi organ failure |

VSD: ventricular septal defect; CoA: Coarctation of the aorta.

Table 6 Risk factors for mortality

| | p-value |
|---|---------|
| Preterm birth | 0.0008 |
| Long duration between cardiac catheterization and surgery | 0.006 |
| Older age at surgery | 0.004 |
| Necessity of associated procedures | 0.004 |
| Redo surgery | 0.04 |
| Prolonged ischemia time | 0.0002 |
| No treatment with prostaglandin prior surgery | 0.002 |

The possible deterioration of neo-aortic valve function with a dilatation of neo-aortic root [7] and presence of coronary stenosis [2] is one of the major concerns of ASO. In the present study, the need of surgical re-intervention of coronary stenosis in the follow up was low (4.5%). Similar results have been described by Bonhoeffer et al. for late stenoses after ASO [10]. In our patient population, 23 of the survivors who have been evaluated by angiography, 2 were found to have complete occlusion of the right coronary artery and 1 had left coronary artery occlusion. The patients with the affected right coronary artery had Yacoub's type E coronary pattern and showed clinical symptoms, which were associated with myocardial ischemia in the year five and seven postoperatively. They were treated surgically with an internal mammary artery grafting, which is one of the possible approaches to manage coronary stenoses after ASO [11]. Although in both patients a good result was achieved with this approach, we recommend a regular follow up by angiography in view of the lack of long-term follow up studies about internal mammary grafting in children. The patient with occluded left coronary artery coronary (Yacoub's type A coronary pattern) was treated conservatively, as the routine angiography revealed a good collateralisation and the patient had no clinical signs of a myocardial ischemia. In the latest follow up, this patient was in functional NYHA class I with no symptoms referable to the cardiovascular system.

Several investigators have noted that a deterioration of neo-aortic valve function and dilatation of neo-aortic root were frequently observed in patients after ASO [12,13]. In the present series two patients developed severe aortic regurgitation (AR) and required an aortic valve replacement at 6 and 8 years after ASO. One of them had a VSD which was also closed during the ASO procedure. Interestingly, both of them had Yacoub's type E coronary pattern and received an internal mammary artery grafting as well, but there is no explanation for the combined occurrence. It was reported that the risk of moderate or severe AR with a significant left ventricular dilatation followed by an aortic valve replacement is low after ASO and the results in this study are similar to other studies [7,13].

Risk factors for AR following ASO included prior history of PA band, Taussig-Bing hearts, and development neo-aortic root enlargement [7]. Surprisingly, in our series the patients with AR who required aortic valve replacement had none of these risk factors. Moreover, we did not observe a neo-aortic root enlargement at all in the follow-up and this is in contrast to other studies which state that that is one of the major concerns of ASO [7]. This could be because of the small size of our series. Although several factors for neo-aortic root enlargement are described, these are speculative and require further investigations. The incidence of pacemaker implantation due to the complete AV block in two and the sick sinus syndrome in one was not different from that in another study [14].

The postoperative mortality and morbidity in this series was higher compared to the recently reported series. We observed an all over mortality rate of 15% (n = 8). The mortality rate seems to be high compared with other published series; however, the mortality was seen only during first 4 years of the observation period which was early nineties. Reasons for that improved outcome after 1994 could be that the ICU treatment made a progress and also the learning curve regarding the surgery has improved in a short time. Moreover, more patients were presented in a better clinical condition in the second time interval.

Seven patients died in the early postoperative period (30 days) and five of them within first 24 hrs. Cause of death was dominated mostly by postoperative refractory left heart failure. In our statistical analysis preterm birth, long duration between cardiac catheterization and surgery, older age at surgery, necessity of associated procedures, redo- surgery, prolonged ischemia, and no treatment with prostaglandin prior surgery were associated with mortality and were partly in line with other published series [6,15]. Maybe it is possible that some of the patients could be supported by an extracorporeal membrane oxygenation (ECMO) in the initial early postoperative phase; however this kind of circulatory support was first introduced in our department in the late nineties.

Interestingly, in our series the presence of a complex coronary anatomy including intramural course was not a significant risk factor for mortality and corroborates with the study of Blume et al. [16]. The results of this study show that the impact of well described risk factors influencing the mortality diminishes with surgical experience. The experience after 1994 has further improved early survival after ASO and may also result in less mid-term complications. After 1994, no postoperative deaths were observed. This result is gratifying and compares favourably with other big series [3,15].

We acknowledge that this study has several limitations being an observational assessment of outcomes. The

patients were not randomly assigned to various therapies, and comparison between inherently dissimilar groups is problematic. Data regarding follow-up and re-interventions were incomplete in some patients; however continued study will be necessary for a truly long-term follow-up.

Conclusion

In conclusion ASO remains the procedure of choice for TGA with acceptable early and late outcome in terms of overall survival and freedom of reoperation. The need for close long-term monitoring in these patients is important to detect any structural changes or changes of hemodynamic which could affect the postoperative result.

Competing interests

There is no undisclosed ethical problem or competing interests related to the submitted manuscript.

Authors' contributions

AP, TT, MG participated in the design of the study and drafted the manuscript. MG, VG, KC participated in the data collection. JH participated in the statistical analysis. GH, TP and WR conceived of the study, participated in its design and coordination, helped to draft the manuscript and give final approval of the version to be published. All authors read and approved the final manuscript.

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