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OROFACIAL CLEFTS AND ASSOCIATED CARDIAC ANOMALIES: THE 18 YEARS EXPERIENCE OF A MULTIDISCIPLINARY GROUP IN A TERTIARY HOSPITAL IN PORTUGAL

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Introduction: Orofacial clefts are a heterogeneous group of disorders arising in about 1.7/1000 newborns. They can occur with other congenital anomalies, including heart disease.

Aim: To describe a population with orofacial clefts and associated cardiac anomalies.

Methods: Retrospective study of patients that attended the Cleft Lip and Palate Multidisciplinary Group at Hospital S. João, Porto-Portugal. Medical records from January-1992 through December-2009 were reviewed. Patients were divided in four groups: cleft lip (CL), cleft lip and palate (CL/P), isolated cleft palate (CP) and atypical cleft (AC). Further categorization included sex, affected relatives, associated congenital anomalies and syndromes.

Results: Of the 340 patients included, 54 (15.9%) presented with cardiac anomalies. Of those with orofacial cleft and cardiac anomalies 55.6% were males and 11.1% had known affected relatives; 59.3% had CP, 27.8% had CL/P, 11.1% had CL and 1.9% had AC. CP was the most common cleft among patients with cardiac anomaly ($p < 0.05$). Additional congenital anomalies were found in 75.9% of patients, facial defects, central nervous system, renal and skeletal malformations were the most common. A recognizable syndrome was identified in 63%, Pierre-Robin ($n=14$) and 22q11.2 microdeletion ($n=9$) syndromes being the most common. Both, additional congenital anomalies and recognizable syndromes were significantly more common in patients with cardiac conditions ($p < 0.05$). The most commonly recorded cardiac anomalies were ventricular septal defect ($n=19$), atrial septal defect ($n=17$) and Fallot's Tetralogy ($n=6$).

Conclusion: Due to the high prevalence of cardiac anomalies, a routine echocardiographic and electrocardiographic screening should be considered in all cleft patients.

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POLYMORPHISMS IN UGT1A1 GENE AMONG NORTH INDIAN NEONATES PRESENTING WITH UNCONJUGATED HYPERBILIRUBINEMIA

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Objective: Genetic factors are implicated in pathogenesis of neonatal hyperbilirubinemia. The present study was conducted to determine the frequency of (TA)_n promoter polymorphism and Gly71Arg mutation in UGT1A1 gene in North Indian neonates ≥ 35 -week gestation presenting with STB ≥ 18 mg/dL and to study the interaction among the presence of UGT1A1 gene polymorphisms, G6PD gene mutations, and peak STB levels.

Methods: In addition to routine tests for jaundice evaluation, DNA was isolated for detection of (TA)_n promoter polymorphism, Gly71Arg mutation in bilirubin UGT1A1 gene and G6PD Mediterranean and Orissa mutations. The number of TA repeats was assessed by a PCR-SSCP analysis and Gly71Arg mutation was detected by PCR-RFLP. Results were confirmed by DNA sequencing in 45 and 50 samples respectively. 127 neonates were enrolled (77 hyperbilirubinemics, 50 controls).

Results: The incidence of (TA)_n polymorphism was higher in babies with hyperbilirubinemia [89.6% vs. 50%, OR 8.63 (95% CI, 3.2-24.1)]. Gly71Arg mutation was not found either in hyperbilirubinemics or controls. Sequencing revealed a novel polymorphism (Ala72Pro) at codon 72 of exon 1 in 21 hyperbilirubinemics and 29 controls. Presence of variant (TA)_n promoter (adjusted OR, 10.6; 95% CI, 3.3-34.2), G6PD deficiency (adjusted OR, 20.6; 95% CI, 3.6-117.3), and history of jaundice in sibling requiring phototherapy (adjusted OR, 12.6; 95% CI, 1.1-141.6) were independent risk factors for bilirubin levels ≥ 18 mg/dL.

Conclusion: (TA)_n promoter polymorphism of bilirubin UGT1A1 gene was significantly associated with hyperbilirubinemia in term and near-term neonates. The effect of novel Ala72Pro mutation on mRNA and protein expression needs to be explored.