**Objective**

To evaluate current practice and diagnostic challenges towards an early prenatal detection of Cornelia-de-Lange syndrome (CdLS).

**Methods**

In this retrospective analysis prenatal records of 8 fetuses of CdLS were analyzed and compared with 98 previously published cases affected by this heterogeneous disorder in order to elaborate common features possibly enabling diagnosis at earlier gestational ages. Primary aim was to sum clinical characteristics regarding potential predominant pattern of CdLS as well as the feasibility of confirmational mutational analysis in fetal life.

**Results**

The average GA at diagnosis was 21.9 weeks (14-37 weeks). The leading prenatal features encompassed micrognathia (7/8), limb reduction defects (6/8) and fetal growth restriction (6/8). In six cases mutational analysis confirmed the final diagnosis of CdLS, in two out of which the diagnosis had been made prenatally. Available additional information revealed that a total of 63/106 cases (59%) had facial anomalies with micrognathia and long philtrum as key features. 64% had different degrees of limb reduction defects, mainly attributed to the upper limbs. 75/106 cases had an FGR as the most striking, but non-specific sign of CdLS.

CHD and diaphragmatic hernia were rather unfrequent findings (15% and 20% respectively) as well as first trimester aneuploidy markers, which is in line with the observation of only 4 cases with chromosomal anomalies in this cohort (3.8%). In about one-third a mutational analysis was positive, exclusively restricted to NIPT gene anomalies – all of those fetuses had above mentioned key features revealing severe type of CdLS.

**Outcome**

Although early diagnosis is feasible as early as 14 weeks, the majority of prenatal cases during mid-second and third trimester, merely driven by the presence of facial and limb anomalies. Until now molecular confirmation of the causative mutation antenatally is scarce and in general restricted to NIPBL gene anomalies.