Prevalence of Intersex Among Egyptian Infants

Thesis

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List of Contents

List of Contents (Cont.)

List of Figures

List of Figures (Cont.)

List of Tables

List of Tables (Cont.)

١. Introduction

The birth of a new baby is one of the most dramatic events in a family, and the first question is usually "is it boy or girl?" The newborn infant with ambiguous genitalia often comes as a surprise to the doctors as well as the parents. The word intersex has conventionally been used to refer to the appearance of the external genitalia being at variance with normal development for either sex ***(Kim and Kim, ٢٠١٢).***

Disorders of sex development are congenital conditions in which development of chromosomal, gonadal or anatomical sex is atypical ***(Garry et al., ٢٠١٢).***

Genitalia is ambiguous whenever there is a difficulty in attributing gender to a child based on the appearance of the external genitalia. Children born with intersex problems comprise about ١,٧٪ of all live births ***(Kumar et al., ٢٠١٢).***

Intersexuality subsumes a wide variety of phenomena with very specific underlying causes. In all cases an untypical development takes place during the prenatal sex differentiation process becoming clinically manifest, either at, or soon after birth or at the time of puberty. It subsumes conditions in which biological sexual characteristics (e.g., Chromosomal sex, gonadal sex, hormonal sex, morphological sex) differs from

each other and one person cannot easily be assigned to one sex ***(Richter-Applet et al., ٢٠٠٥).***

Disorders of sex development can be subdivided into three main groups: disorders associated with gonadal dysgensis, disorders associated with under virilization of ٤٦,XY individuals and disorders associated with prenatal, and possibly also postnatal virilization of ٤٦, XX subjects ***(Warne et al., ٢٠٠٨).***

Hutcheson and Snyder (٢٠٠٩) mentioned that intersex traditionally divided into five simplified classifications based on differentiation of gonads, female pseudohermaphroditism (two ovaries), male pseudohermaphroditism (two testis), true hermaphhroditism (ovary and/or testis/or ovotestis) mixed gonadal dysgenesis (testis plus streak gonad), pure gonadal dysgensis (bilateral streak gonads).

Disorders of sex development have a broad range of underlying causes in Egypt with some preference of rare monogenic disorders. For improving diagnostic standards, the provision of tertiary pediatric care is recommended for patients with disorders of sex development even in developing countries ***(Mazen et al., ٢٠٠٨).***

A new born with ambiguous genitalia needs prompt evaluation to detect life threatening conditions (e.g Salt losing

crises in congenital adrenal hyperplasia) and gender assignment in these children continues to be a challenging diagnostic and therapeutic problem ***(Almutair, ٢٠٠٤).***

٢. Aim of the Work

The aim of this study is to survey the prevalence of intersex cases among Egyptian infants and record the different types of intersex.

٣.١. Intersex and Sexual Differentiation

When a child is born, most often the first question asked is: Boy or girl? From that moment forward, our sex, whether we are male or female, influences almost every aspect of who we are and how we live. But how deep are the differences between males and females, and how do these differences come about? These questions seem at first glance rather simple, but in fact they are stunningly complex ***(Wilhelm et al., ٢٠٠٧).***

٣.١.١. Intersex Definition

Intersex is defined as incomplete or disordered genital or gonadal development leading to a discordance between genetic sex, gonadal sex, and phenotypic sex. Together, disorders of sex development (DSD) form a complex entity of heterogeneous etiology that affect the four different dimensions (genetic sex, gonadal sex, phenotypic sex, and behavioral sex) of sex development ***(Cool et al., ٢٠٠٦).***

There is a wide range of conditions with diverse pathophysiology that most often present in the newborn or the adolescent. Affected newborns usually present with atypical genitalia whereas adolescents present with atypical sexual development during the pubertal years. These clinical situations

can often be difficult to manage, particularly in those cases where the sex of rearing is uncertain ***(Ahmed et al., ٢٠١١).***

Ambiguous external genitalia (AEG) are manifestations of Disorders of Sex Development (DSD). It is a term used to describe individuals whose external genitalia is deviant from the normal (intersex) with failure to categorize the sex of the child from the appearance of the external genitalia ***(Anochie et al., ٢٠١١).***

In response to concerns regarding outdated, confusing and/or controversial terms, such as "intersex," "hermaphroditism" and "sex reversal," the Chicago consensus statement recommended a new taxonomy based on the umbrella term, disorders of sex differentiation ***(Barthold, ٢٠١١).***

٣.١,٢. Male and Female Sexual Differentiation

Sexual differentiation fundamental results from chromosomal differences, because males (typically ٤٦, XY) and females (٤٦, XX) are defined by the presence or absence of a Y chromosome ***(Wilson and Davies, ٢٠٠٧).***

There is a growing body of knowledge related to the genes that control sex determination and differentiation. In the initial stage of gonadal development the genetic control does not differ in either gender. Regulatory genes controlling the development of the genital ridge and the formation of the

bipotent gonad have been identified and developmental anomalies resulting from gene mutations have been described ***(MacLaughlin and Donahoe, ٢٠٠٤).***

The differentiation of the bipotent gonad to an ovary or testis follows and is also under genetic control. Several genes affecting testicular differentiation have been determined, whereas very little is known about ovarian formation. Since a functioning ovary is not necessary for female phenotype development, while a testis are necessary for the male phenotype, the development of the ovary has been incorrectly considered a development by 'default'. The author has suggested that specific genes are required for the early development of the ovary and that mutations in these genes influences ovarian development and result in specific clinical syndromes ***(Hughes, ٢٠٠٤).***

Fetal sex development consists of three sequential stages: a) the undifferentiated stage, when identical primitive structures develop in the XY and XX embryos, b) gonadal differentiation into testes or ovaries, and c) the differentiation of internal and external genitalia, which depends on the action of testicular hormones. Disorders of sex development (DSD) may result from defects in any of these stages ***(Rey et al., ٢٠١١).***

٣,١,٢,١. Basic embryology of the ovary and ducts:

The urogenital ridge, from which the urogenital system will derive, rises at approximately the ٤th week of gestation in

the intermediate mesoderm. The indifferent gonad, identical in females and males, emerges on the ventromedial surface of the mesonephros as a derivative of the intermediate mesoderm. The indifferent or bipotent gonad is formed by proliferation of the coelomic epithelium and a condensation of mesenchymal cells of mesonephric origin. Primordial germ cells (PGCs) derive from the epiblast, the outer ectodermal layer of the embryo; they subsequently move to the yolk sac wall and then migrate along the dorsal mesentery of the hind gut to the gonadal ridge (Figure ١). During the migration, PGCs undergo cell division and, once in the genital ridge (by the end of the ٥th week), lose their motility, begin to aggregate and continue to proliferate by mitosis ***(Sadler, ٢٠٠٦).***

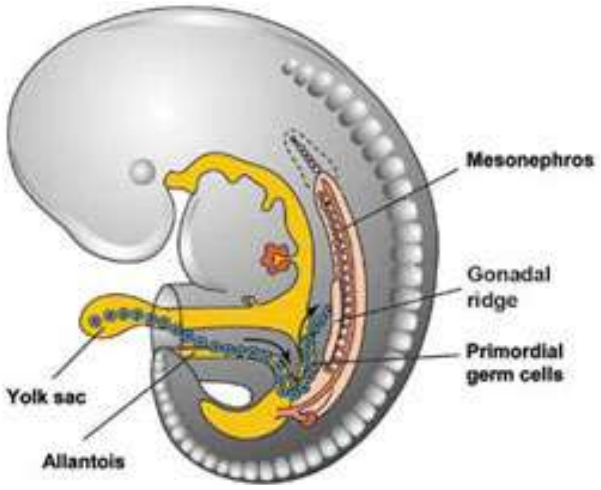

Figure (١): Embryology of ovary. The gonad emerges on the ventromedial surface of the mesonephros at the ٤th week of gestation. The migration of the primordial germ cells (PGCS) from the wall of the yolk sac along the dorsal mesentery of the hind gut to the gonadal ridge is shown as blue circles ***(Kousta et al., ٢٠١٠).***