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REVIEW ARTICLE

Pediatric and adolescent gynecology through a global lens

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Synopsis

This article will highlight common gynecologic conditions of adolescents, and will also present social determinants to improve reproductive health.

Abstract

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Girls and adolescents, aged 0-19 years make up almost 30% of the world population yet their specific health care needs often slip between the gaps of pediatrics and adult women's health.

Pediatric and adolescent gynecology is the clinical field that endeavors to address the reproductive health needs of this age group. The environment and psychosocial wellbeing, social determinants of health, have direct bearing on reproductive health, affecting menstrual cycles, menstrual hygiene and risks for unintended pregnancy and sexually transmitted infections. This narrative review will highlight common gynecologic conditions of adolescents, especially where diagnosis and management are distinct from adult women. It will also present preventative health strategies to improve reproductive health through vaccination, improved access to hygiene supplies and contraception.

1 Introduction

Girls and adolescents, aged 0-19 years make up almost 30% of the world's population [1] yet their specific health care needs often slip between the gaps of pediatrics and adult women's health. There are gynecological conditions that are specific to this age group; yet receive little attention during postgraduate training in pediatrics or obstetrics and gynecology. On an individual patient level, the management of common problems, for example irregular periods, often requires a different approach to that of adults. On a systemic and even global level, mitigation of factors such as disproportionately limited education opportunities, with outsized impact of climate change and social crisis is needed to improve welfare of this vulnerable population.

Pediatric and adolescent gynecology is the clinical field that endeavors to address the reproductive health and wellbeing of this age group [2]. As with all clinical care, this needs to be embedded in the psychosocial as well as environmental needs of the young **person**, including the social determinants of health.

This narrative review will address a number of reasons why the reproductive health needs of this age group are different from those of adult women, and will provide strategies that when addressed in adolescence, can improve lifelong health.

2 Common gynecologic disorders may have a different etiology and management in adolescents

Adolescent girls may present to the healthcare providers for a variety of reproductive health concerns, including menstrual irregularities, pelvic pain, pelvic masses, and vulvar disorders, and the underlying pathology of these disorders in girls is often different from those of older adult women. Understanding the differences in pathophysiology between adult and pediatric reproductive health concerns can help guide appropriate management, preserve reproductive abilities and improve the overall health of the adolescent girl.

3 Menstrual Disorders

One of the most common complaints in pediatric and adolescent gynecology is abnormal bleeding. Understanding normal bleeding patterns in adolescents is key to recognizing menstrual disorders. Globally, the average age of menarche is 12-13 years. While a recent study confirms that many cycles in the first few years after menarche can be anovulatory due to an immature hypothalamic pituitary access, 90% of cycles are usually 21-45 days in length [3,4]. Infrequent menses in the first post-menarchal year is defined as having fewer than 4 menses, and often can be attributed to neuroendocrine immaturity and anovulation [5]. It is, however, uncommon for adolescent patients to remain amenorrheic for more than 3 months, warranting evaluation [3]. For an overview, see table 1.

The etiology of amenorrhea, aside other than teenage pregnancy, depends on both primary and secondary causes. Malnutrition is a cause of secondary amenorrhea in adolescents that has global significance. Globally, the prevalence of severe food insecurity is higher among women than men and more than 120 million women in less developed countries are underweight [6]. Malnutrition or states of undernutrition as in anorexia nervosa cause deficiency of fat stores as an energy source, lower leptin levels, and endorphin suppression of gonadotropin release, leading to anovulation and disruption in menstruation [5]. Decreased energy availability seen in some competitive athletes (RED-S, relative energy deficiency in sports) also causes hypothalamic hypogonadism. In addition to amenorrhea, the low estrogen levels in these girls combined with the relatively low energy availability causes decreased bone density at a critical time of bone mass development [7]. Treatment for amenorrhea from undernutrition disorders and for relative energy deficiency should

be tailored to restoring a balanced pattern of eating and energy expenditure with the goal of restoring menstruation as a clinical marker of nutrition status and energy balance [3,8].

The diagnosis of polycystic ovary syndrome (PCOS) in adolescents, as a cause of infrequent menses, should be made with caution. Overdiagnosis and labeling can lead to unnecessary interventions. Anovulatory cycles, elevated levels of androgens from adrenarche producing acne, and even the PCO ovarian morphology can be seen in normal girls. Worldwide adolescent obesity has risen from 4% in 1975 to over 18% in 2016. Obesity, insulin resistance and hyperinsulinemia may contribute to the metabolic abnormalities of PCOS, and should prompt screening for diabetes and healthy lifestyle counseling, but are not diagnostic criteria for PCOS [9]. Significant hirsutism, >95% of the population norm, persistent severe acne, clitoromegaly should prompt androgen testing to rule out nonclassical congenital adrenal hyperplasia and tumors. In adolescents diagnosed with PCOS or at risk for PCOS, lifestyle modification, with the addition of combined oral contraceptives and metformin in patients with hyperinsulinemia, can be used [9].

Adolescents may also present for management of heavy menstrual bleeding (HMB), defined as excessive blood loss that interferes with quality of life. Abnormal uterine bleeding is typically classified using the PALM-COEIN system: Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, latrogenic, and Not otherwise classified [10]. Structural causes of bleeding are uncommon in the adult population; the main etiologies of concern in this population are most often due to anovulatory bleeding (see figure 1), and underlying bleeding disorders. Heavy menstrual bleeding (HMB) at menarche or in adolescence can often be the presenting symptom for an underlying bleeding disorder. Nearly 20% of adolescent girls who present with HMB at menarche or in adolescence are found to have an underlying bleeding disorder [10]. The most common of these bleeding disorders include von Willebrand disease, platelet function defects, and thrombocytopenia. Screening questions should include risk factors for bleeding disorders, see table 2. Management of acute HMB depends on hemodynamic stability of the patient but typically involves hormonal and nonhormonal management [10]. Continuous or extended cycle combined oral contraceptives, depomedroxyprogesterone acetate (DMPA) and levonorgestrel intrauterine devices are all effective in reducing bleeding and can be used in adolescents with heavy bleeding

including those who are not sexually active. Where families are uncomfortable with prescription contraceptives or where estrogen must be avoided, continuous oral norethindrone, also known as norethisterone acetate, (5-10 mg) may be acceptable. Tranexamic acid also reduces menstrual blood loss in adolescents and can be combined with hormonal therapy [10].

4 Dysmenorrhea and pelvic pain

Dysmenorrhea, or menstrual pain, is a highly prevalent menstrual symptom, occurring in 50-90% of adolescent girls [11]. Dysmenorrhea can be defined as either primary or secondary. Primary dysmenorrhea typically occurs in adolescents within 6-12 months of menarche, when ovulatory cycles begin, and is usually due to increased activity of inflammatory mediators like prostaglandins and leukotrienes [11]. Management includes use of timed non-steroidal anti-inflammatory drugs or hormonal therapy to decrease prostaglandin release [11]. The most common cause of secondary dysmenorrhea in the adolescent population is endometriosis with an estimated prevalence of approximately 60% in patients with persistent dysmenorrhea or pelvic pain not responding to medical management [12]. Management goals of endometriosis in adolescents include symptom relief, suppression of disease progression, and protection of future fertility. In all girls with dysmenorrhea and pelvic pain, management of the presenting pain should include identification of potential contributing factors for the pain experience (such as adverse childhood events and abuse) and early diagnosis of the comorbid pain conditions such as irritable bowel, headaches, abdominal wall / musculoskeletal related symptoms and central pain sensitization allows the opportunity for early and appropriate interventions. While endometriosis is a surgical diagnosis, appearance of lesions differs between adolescents and adults. In adolescents with earlier disease, the metabolically active prostaglandin-producing, lesions are clear or red and may require enhanced visualization techniques to identify, including magnification and saline use [11]. These lesions are also known to be more metabolically active and associated with greater prostaglandin production, therefore adolescent patients may experience more substantial pain than with the typical "powder burn" lesions seen in adult women [11]. Visualized lesions should be ablated or excised with the most conservative surgical technique to prevent adhesion formation. Undertaking a laparoscopy to make the lesion-focused diagnosis and to treat superficial peritoneal

lesions is not considered standard of care universally as the progression from mild to more severe disease in the absence of surgical management is not clear. The mainstay management of endometriosis for adolescents is conservative, with suppressive hormonal therapy to prevent endometrial proliferation [11,12]. Reproductive tract anomalies associated with complete or partial obstruction to menstrual flow can also be suspected in cases of adolescent secondary dysmenorrhea, amenorrhea, pelvic pain, or recurrent vaginal discharge refractory to medical management.

5 Adnexal Masses

Ovarian masses in the pediatric and adolescent population can be found incidentally on imaging or may present with pain, menstrual irregularities, or signs of precocious puberty [13]. Most ovarian masses in pediatric and adolescent patients are physiologic or benign. Of ovarian lesions managed operatively, the reported rate of malignancy is 10%–20% which comprises approximately 1%–2% of all childhood malignancies [14]. A Decision Tree System has been proposed to aid determination of which masses are malignant prior to surgery, using a morphology index and ovarian crescent sign, while other studies have shown that using a measurement of 8 cm or greater with a complex/solid appearance of the mass predict a higher risk of malignancy [15,16]. Management of benign ovarian masses should be ovariansparing, typically through laparoscopy, which provides the best outcome in terms of fertility preservation and minimization of tissue damage [15].

Timely diagnosis of adnexal torsion is paramount to preserve fertility. Adnexal torsion can be due to functional cysts, such as hemorrhagic corpus lutea, or paratubal cysts or mature cystic teratomas. The most common presentation is intermittent pelvic pain, associated with nausea and vomiting in 66% of patients. Ultrasonography may show a unilaterally enlarged ovary, with edema and peripheral follicles. It is important to note that doppler flow is not sensitive in predicting torsion, and prompt surgical intervention is needed to preserve ovarian function [17]. The preferred management is detorsion, not oophorectomy, even if the ovary appears dark and ischemic, as studies have shown that follicular function can be found with detorsion of ovaries previously suspected of being nonviable. There is no increased morbidity (neither infection nor thromboembolism) with detorsion and retention of the ovary [17].

Oophoropexy is controversial and is usually recommended only for 2-12% patients with recurrent torsion [18].

6 Maternal mortality and morbidity are increased in adolescents

Adolescent pregnancy is a global problem that occurs across the continents in high-, middle- and low-income countries. It is estimated that 21 million adolescent girls aged 15 to 19 years and two million under the age 15 become pregnant each year. Approximately 16 million girls aged 15 to 19 years and 2.5 million girls under age 16 years annually give birth in developing regions [19]. While many countries have policies aiming to decrease the rates of adolescent pregnancy, much progress is still needed. Rates of adolescent pregnancy have only been slowly declining in Africa, and are still rising in the Asia-Pacific region [20].

Across all income regions in the world, perinatal morbidity and mortality is increased in pregnant adolescents compared to adult pregnant women. According to WHO, pregnancy and childbirth complications are the second leading cause of death amongst 15- to 19-year old girls with approximately 70,000 adolescents dying annually [21]. Pregnancy associated mortality is about a third higher among 15- to 19-year-olds than among 20- to 24-year-olds [22]. Adolescent mothers are at higher risk of pregnancy complications and adverse pregnancy outcomes including pre-eclampsia, obstructed labor, and postpartum fistula. Poor nutritional status and social stressors in adolescent mothers can also cause low infant birth weight and increased perinatal morbidity [23-24].

In 2011, the World Health Organization (WHO) and the United Nations Population Fund (UNFPA) published guidelines on preventing adolescent pregnancy and poor reproductive outcomes in developing countries, which set out clear recommendations, on increasing access to and uptake of contraception, based on the studies of the effectiveness of research studies and projects from around to work [25]. Chile and Ethiopia are great examples of successful programs. Both countries legalized the provision of contraception to adolescents through national policies and strategies; they built adolescent demand for contraceptive services and community support for their provision. They also overcame barriers to access by expanding the provision of contraceptive services by strengthening (and in the case of Ethiopia, expanding) the delivery system. Barriers to provision of care for adolescents remain in countries where marriage is a requirement for contraceptive services.

7 Sexually transmitted infections are common in adolescents

High risk sexual activity exposes adolescents to sexually transmitted infections (STIs). WHO has estimated 333 million curable STI's occur each year [26]. Globally, adolescents comprise at least one third of chlamydia trichomatis infection. Coinfection of chlamydia and gonorrhoea is common. Adolescents also account for a high number of cases in trichomonas and herpes genitalis [27]. Prevention strategies for all STIs, include broad education about condom use and increasing condom availability, is vital [26]. Multiple STIs can occur concurrently in adolescents with high risk behavior, and remain asymptomatic in infected individuals. Screening for STIs, including HIV, in this population is important to identify individuals to implement life-saving antiviral therapy. Untreated STIs can cause pelvic inflammatory disease, chronic pelvic pain, ectopic pregnancy, and tubal infertility.

8 Providing HPV vaccination to prevent cervical cancer

Human papillomavirus (HPV) infection exposure begins with sexual activity in adolescence and young women, and increases the risk of cervical cancer later in life. While often transient in young women, and screening should be avoided in adolescents to reduce overtreatment, prevention with vaccination is key to reducing infection and lifelong sequela. The HPV vaccine was introduced in 2006 and the WHO recommends all children be vaccinated routinely at 11 or 12 years of age. However, social and economic inequity exists in vaccine access [28-29]. The vaccine uptake differs across the global regions, 28% of girls aged 10-14 years are reported to have received HPV vaccination in North America, 40% in Latin America, 3% in Eastern Africa, 18% in South Africa, 46% in Northern Europe and 41% in Australia and New Zealand [30].

Strategies that have been shown to increase HPV vaccination rates, include implementation of public health and government policies, health education and health promotion programs, and clinical and patient-provider approaches. Pro-active work aims to respond to and combat anti-HPV vaccination movements in society [29]. Despite 100 countries now having the HPV vaccine in their national schedules, the coverage has remained lower than for other vaccines recommended for adolescents. This is believed to reflect parental hesitancy for vaccination; parental

education on vaccine safety and efficacy results in greater likelihood of their children receiving the HPV vaccine [31]. An effective approach to increase HPV vaccination is delivery of vaccination in schools, as demonstrated by Australia and the United Kingdom, who have vaccine completion rates among 11-to-12-year-old girls exceeding 80% [28]. eHealth technologies provide an opportunity to address HPV vaccination initiation and completion through quality improvement metrics of provider practices.

9 Addressing the social determinants of health is key to improving the reproductive health of adolescents

The health of young people is determined as much by the environment, psychosocial and physical, as it is by underlying medical conditions. Politics, culture, family norms and religion have an impact in adolescent health in different ways. The availability of sexual and reproductive healthcare is recognized as a health and human rights issue, just as violence against girls. Politicians can positively influence the social determinants of health by prioritizing primary education, improvement of maternal health, healthcare accessibility to promote gender equality and empowerment of women [31]. These strategies for improved adolescent health through providing access to comprehensive reproductive health education, preventative services as HPV vaccination programs, access to contraception and abortion care, as well as attention to the environment, like role of parents in facilitating or hindering access, are necessary for a sustained positive impact [32]. In many countries sound national adolescent sexual reproductive health strategies already exist. However, these measures are not always implemented. Personal bias, grounded in religion or tradition, combined with religious and cultural influences can act as barriers to implementation of policies and strategies at district, provincial and sub-national levels. Requirements for parental permission to access services, and parental refusal of reproductive health care can negatively impact adolescent health.

10 Empowering girls through education

Structural racism, poverty, and patriarchy have directly affected the reproductive health care of women for millennia. Education attainment is closely tied to the overall health in girls. When provided the opportunity to attain higher levels of education, adolescent girls are less likely to have early and unintended pregnancies [33]. As noted in the UNESCO report, which demonstrates each additional year of education is associated with 10% reduction in unintended pregnancy [33]. As a result of one of the millennium development goals [34], improved school retention has occurred in some global regions such as Sub Saharan Africa and South Asia. Indicators to monitor the progress include not only the literacy rate, rate of girls in primary, secondary and tertiary education, but also reproductive health metrics such as adolescent birth rate and contraceptive prevalence rate [21]. In some cultures, there is social pressure to get married young and bear children. As a consequence of early marriage, delay and absence from school, girls attain lower education and skills, and have limited job opportunities [34]. This also leads to increased rates of unintended pregnancy. The lack of autonomy and financial independence further limit the ability of adolescent girls to seek healthcare, including contraceptive, services, protection from threats of exploitation or even violence, including female genital mutilation. The problem often propagates intergenerational poverty, therefore every effort should be made to keep girls in school. Young mothers may be unprepared, physically and physiologically, for parenthood. Adolescents given autonomy over their reproductive health require education to make informed decisions about their health. Flexible education, parenting skills training as well as emotional support can help adolescent mothers become successful [35].

11 The impact of climate change on the health of girls

The Lancet Countdown on climate [36] change summarizes the situation with regard to climate change concluding that a "business as usual trajectory will result in a fundamentally altered world. The life of every child born today will be profoundly affected by climate change". By 2030–2050, between 250 000–400 000 extra deaths per year are predicted to occur due to malnutrition, malaria, diarrhea and heat stress [37]. The impact of climate change will threaten all development and health gains of the past 50 years and threatens to put 30% of the world population back into extreme poverty [38-40]. The number of weather-related disasters has tripled since the 1960s [37]. To date, 93% of the world's children live in areas where particulate matter levels are above WHO air quality guidelines [40]. Air pollution is a cause of exacerbation of lung diseases including asthma, elevated pregnancy risks

including low birth weight and prematurity, as well as slower attainment developmental milestones and reduced cognitive function [41-42]. Climate change acts as a risk multiplier, making vulnerable groups more vulnerable, as these are the very people who have the least capacity to adapt. It is a gendered issue as the impact is greater on girls than boys [39]. Girls make up a greater proportion of deaths/disability during cyclones and floods- as they are often not taught to swim, are obliged to stay in the house as they are responsible for the household and livestock, and not clothed in a way that enables rapid movement. Sexual abuse/harassment are increased following crises and disasters when families and societies are under stress. Girls are removed from schools to do paid labor following disasters when the families are in financial strife, or they may be sold into marriage, or sex trafficking.

12 Addressing Gender based violence

Gender based violence (GBV) is any harmful act (physical, sexual or mental), threat, coercion that is perpetrated against a person's will based on gender differences [43]. GBV occurs in girls due to the subordinate status in society, a form of gender inequality. The maintenance of privileges, power and control of others in certain cultures may be displayed through acts of GBV. Cultures are not a static phenomenon; they are continually being renewed and reshaped by a wide range of factors, and decreasing the gender power differential within a culture can improve the social determinants of health [43].

Examples of GBV range from child sexual abuse to child marriage, female genital mutilation, rape or sex trafficking. The most extreme form of gender-based violence includes female infanticide, honor killings and femicide. In the world, this occurs on a vast scale. Globally, it has been estimated that child sexual abuse has a prevalence of 2-62% and annually more than 2 million girls will undergo female genital mutilation/ cutting (FGM/C) [44]. FGM is more prevalent in some parts of the world than others.

13 Improving reproductive health by access to sexual and reproductive healthcare services

The United Nations has a recognized the human right of girls to decide how many and when she wants to have children, and to attain the highest possible standard of sexual and reproductive healthcare. The United Nations 2030 Agenda for Sustainable Development, Target 3.7, which states that countries should, "by 2030, ensure universal access to sexual and reproductive health-care services, including for Family Planning (FP), information and education, and the integration of reproductive health, into national strategies and programs" [45].

The use of long-acting reversible contraceptives (LARCS), the contraceptive implant and intrauterine devices, is safe in adolescents and effectively reduces unplanned pregnancies. LARCS have higher efficacy, continuation rates, and satisfaction rates compared with short-acting contraceptives among adolescents. Barriers to use of LARC by adolescents include patients' lack of familiarity with or understanding about the methods, potentially high cost of initiation, lack of access, low parental acceptance, and healthcare providers' misconceptions about the safety of LARC use in adolescents. Because adolescents are at higher risk of STIs, adolescents, who choose LARC methods, should also be taught to also use male or female condoms consistently (dual method use) to decrease the risk of STIs [46]. Immediate postpartum provision of LARCS can prevent recurrent subsequent adolescent pregnancy and increase spacing of pregnancies.

To increase contraceptive access, short-term combined oral contraception (COC) can be prescribed through telemedicine without an in-person visit [47]. The quick start of short-term hormonal contraception methods allows girls to start the method at any time, regardless of when her last period and last sexual encounter occurred. This is particularly beneficial for adolescents who can be instructed to start a method on the day of the consultation.

Emergency contraception (EC) should be made widely available for young women who have had sex without contraception, including incidents of rape and assault. These include many methods such as the copper IUD, levonorgestrel 1.5 mg, ulipristal 30 mg, and COCs as part of the Yuzpe method [48]. Not all of them are available in all countries. The use of EC, as soon as possible after sex, prevents ovulation at the earliest possible time. All these EC methods do not affect an already implanted embryo and are not considered abortifacients [48].

On a global scale, three out of 10 pregnancies end in an induced abortion. Every year, about 3.2 million girls aged 15-19 years undergo abortion worldwide [25]. As many as half of all pregnancies end in abortion, whether abortion is restricted or broadly legal, often occurring in developing countries [49]. Therefore, it is essential to

provide adequate resources and appropriate knowledge to adolescents for access to safe abortion services.

In conclusion, health care providers, especially the Obstetrician-Gynecologist, can positively impact the health and wellness of adolescent girls through identification and management of common gynecologic conditions presenting in adolescents, and provision of preventative health services, such as contraception and HPV vaccination. Through awareness of the impact of social determinants of health, and advocacy of the medical community to support education for girls and accessible sexual and reproductive healthcare facilities, providers can insure the best possible future for our girls.

Author contributions

EJR: design, planning, conduct, manuscript writing and editing.

JSC: design, planning, conduct, manuscript writing and editing.

CC: manuscript writing and editing.

DL: manuscript writing.

SG: manuscript writing and editing.

Conflicts of interest

All authors have no conflicts of interest.

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Figure Legend

Figure 1. [Author: Please provide a title for this figure.]

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TABLE 1. Evaluation of the Adolescent Patient with Amenorrhea and InfrequentMenses (cycle length greater than every 3 months)

Disorder	Evaluation	Management
Hypothalamic hypogonadism: Undernourished/low body mass	Hormone assays: low follicle stimulating hormone (FSH). low	Treat anorexia Nutritional rehabilitation
index: Relative Energy	estradiol	
Deficiency in Sports (also	Bone densitometry (DEXA)	Consider physiologic hormones
known as female athletic triad),		(estradiol/progesterone) if
anorexia nervosa		significant bone loss
Pituitary insufficiency		
Premature ovarian insufficiency	Hormone assay: Elevated FSH, low estradiol	Physiologic hormone replacement
Polycystic ovary syndrome	Hormonal assays: Elevated	Weight loss in obese patients
(current global guideline	testosterone (total or free)	Combination oral
suggests diagnosis should not	Screen for diabetes, but	contraceptives
be made within 5 years of	hyperinsulinemia not part of the	Metformin in patients with
menarche [9]): infrequent	diagnostic criteria	hyperinsulinemia
menses with hirsutism		

TABLE 2. Evaluation of HMB in nonpregnant adolescents

Screening questions	Menstrual History: Duration of menstrual bleeding > 7days, gushing or flooding of blood, bleeding through tampon or sanitary pad in less than 2 hours, General medical history: Treatment for anemia, bleeding after dental or surgical procedures or delivery Family history: Bleeding disorders, maternal history of heavy menses or postpartum hemorrhage
Laboratory evaluation to assess heavy bleeding	Complete blood count with platelet Serum ferritin Prothrombin and partial thromboplastin

	times Fibrinogen Von Willebrand Antigen and Activity, Factor VIII level
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Fig Abnormal Bleeding from Anovulation in Adolescents

