Ovarian hyperstimulation syndrome (OHSS) is a well-known iatrogenic condition, considered to be one of the most serious complications of controlled ovarian hyperstimulation (COH), observed during in vitro fertilisation (IVF) treatment. Its manifestations alongside other disease conditions have been mentioned in many case reports, but not with schistosomiasis. We herein present the case of a 33 year old, P1 + 0 woman with features of moderate OHSS during IVF treatment and subsequently diagnosed with schistosomiasis. Both conditions were treated and resumed to the fertility clinic two months later where frozen embryo replacement was planned for her, using a natural cycle and two embryos were put back. She became pregnant and made good progress with her antenatal. Extensive review of literature showed that schistosomiasis was not reported in association with OHSS; our case report presents an instructive guide to clinicians to always look beyond surgical complications such as bladder and ureteric injuries in IVF patients.

Keywords: IVF, moderate OHSS, *schistosoma haematobium*, urinalysis

### Introduction

Ovarian hyperstimulation syndrome (OHSS) is a well-known iatrogenic condition, considered to be one of the most serious complications of controlled ovarian hyperstimulation (COH), observed during in vitro fertilisation (IVF) treatment. OHSS, although regarded as rare, but its severe form is life threatening. Studies have classified the manifestations of OHSS into three forms based on clinical and laboratory parameters. It may occur as mild OHSS, characterized by enlarged ovaries, abdominal distension with possible nausea and emesis. While moderate OHSS presents additional accumulation of ascites, clinically the severe or critical form of OHSS is characterized by evidence of ascites, vomiting and diarrhea, potential renal insufficiency, hemorrhocentration and thromboembolic phenomenon. Mild OHSS is reported to occur in up to 33% of IVF cycles, moderate OHSS in 3% to 8%, while severe OHSS occur in 0.5-5% of IVF cycles with a mortality rate of about 1 in 50,000. Predisposing risk factors to OHSS include history of previous OHSS, atopy or allergies, polycystic ovarian disease (PCOD), young age and low body weight. The pathophysiology of OHSS is still been hypothesized from the studies of Tollan *et al.* and Goldsman *et al.* They explained the release of vasoactive mediators from hyperstimulated ovaries. This leads to increased capillary permeability causing the extravasation of fluid from the intravascular compartment into the third space. Consequently, haemocoencentration ensues and complications such as hypercoagulability and reduced end organ perfusion. In a recent review by Smith *et al.*, the role of human chorionic gonadotrophin (hCG) was implicated in OHSS through mediating the release of vascular endothelial growth factor-A (VEGF-A) and the intraovarian renin angiotensin system (RAS). This was supported by the earlier findings of functioning FSH-secreting pituitary macroadenoma study by Macchia *et al.*

Schistosoma haematobium is the earliest identified digenetic trematode, a tropical disease mainly associated with urinary schistosomiasis, strongly associated with bladder...
cancer\(^{[13]}\) that threatens human health, especially in Africa. There is no literature, following extensive search on African Index Medicus, PubMed and the Cochrane Library that evaluated the incidence of *Schistosomiasis* in patients with OHSS. In this case report we discuss the potential disguise for *Schistosomiasis* as bladder injury in patients diagnosed with OHSS.

## Case Report

A 33yr old p1 + 0 presented to the fertility clinic on account of secondary infertility, having had her last child birth 5 years prior to presentation. Physical examination was unremarkable and she menstruates for 5 days in a regular cycle of 30 days interval. There are no previous surgeries but hysterosalpingogram (HSG) done showed a bilateral tubal blockage. A transvaginal scan showed normal uterus, good endometrium with polycystic ovaries. Her hormone profile was within normal limits except prolactin levels which were elevated and she was promptly placed on cabergolin. Her husband’s seminal analysis showed 6 million count, 50% motility with 4% normal forms. She was started on a short antagonist protocol and was stimulated with FOLLIGRAF\(^{TM}\) 225IU on her 3\(^{rd}\) day of menstruation for 10 days with cetrodine 0.25mg commenced when her lead follicles was 12mm. She had 10 follicles on the right and 8 follicles on the left and she was triggered with 10000IU of PREGNYL\(^{\text{R}}\). Oocytes retrieval was 36hours later and 12 eggs were retrieved. Four days after OCR, she developed moderate OHSS and her embryos were frozen.

She presented 2 days later with complaints of abdominal pain, bloated abdomen and a history of haematuria. She was promptly admitted with a working diagnosis of moderate OHSS and commenced on intravenous fluid; Ringers lactate alternating with Normal saline, with a strict input/output monitoring, daily abdominal girth measurement and she was subsequently catheterised. Full blood count (FBC), creatinine (E/U/Cr) and urinalysis were ordered and packed cell volume (PCV) was 41% with other parameters within normal limits. E/U/Cr was also within normal parameters. A transabdominal scan done showed normal sized uterus, thick endometrium and bilaterally enlarged ovaries with cystic masses of varying sizes and texture. Urinary bladder empty but with pocket of urine with internal echo noted.

2 days after admission, Total haematuria associated with clots were noticed in the urine bag, but there was associated dysuria and no fever. She was reviewed by the Nephrologist and Urologist where she did not give any previous history of gross haematuria. Blood samples for the international normalized ratio (INR), prothrombin time (PT) and partial thromboplastin time (PTT), were collected and a urine microscopy was also ordered. By the 3\(^{rd}\) day on admission, she was noticed to be in stable condition but still passing frank haematuria in the urine bag. Abdominal girth was not increasing and PCV level was 38% but other parameters were still within normal limit. INR, PT and PTTK were also within normal range but interestingly, urine microscopy yielded ova of schistosoma haematobium. She later admitted a positive history of exposure to streams and pond. She was placed on Tabs Praziquantel (CYSTICIDE\(^{\text{R}}\), 3 tablets stat to be repeated in a week) and liberal fluid intake was encouraged. By the 4\(^{th}\) day on admission, she was very stable and urine was becoming clearer in the urine bag. The catheter was eventually removed and her next urine sample was devoid of any trace of haematuria. Within the next 24 hours she made significant improvement, her repeated PCV was 38\%, urinalysis was normal and she was subsequently discharged.

She presented two months later to the fertility clinic where a frozen embryo replacement was planned for her, using a natural cycle and two embryos were put back. Pregnancy test two weeks later was positive. There was no sign of OHSS and she has made good progress with her antenatal.

## Discussions

The initial concern of the authors was bladder or ureteral injuries that have been documented to occur in cases following oocytes retrievals during IVF treatment.\(^{[15,16]}\)\)\) but this was not the case, rather it was *Schistosoma haematobium*. It is well documented that about 85% of the 800 million people at risk of *Schistosoma haematobium* live in Africa.\(^{[17]}\) In Nigeria, *Schistosoma haematobium* and *S. mansoni* has existed since 1881.\(^{[18]}\) The prevalence of *S. haematobium* infection in Nigeria ranges between 70 million and 10 million people suffering from haematuria to bladder wall pathology and hydronephrosis respectively. Contact with cercariae contaminated river, lake and pond water is the major risk factor of *S. haematobium* infection\(^{[19]}\) as confirmed by the patient. However, *S. haematobium* ova in the female genital mucosa have been discussed. Spectacularly this infection has also been misdiagnosed as tuberculosis or tumor of the bladder in migrants from Africa.\(^{[14]}\)

The key to prevention of OHSS include the proper identification of the population at risk, such as enumerated above, which also includes women with high serum estradiol (E2) before hCG administration (E2 >4,000 pg/mL) and multiple follicular response (>35)\(^{[5]}\)\) thus the valuable implication of Anti-Müllerian Hormone and the antral follicle count.\(^{[11]}\) While the role of radiology such as ultrasound scan is of utmost importance not only in diagnosing OHSS,\(^{[20]}\) the management of OHSS primarily consists of supportive and close monitoring of volume status strategy, judicious fluid therapy, prophylactic or therapeutic anti-coagulation, ventilatory support and therapeutic paracentesis to relieves intra-abdominal pressure.\(^{[4]}\) Other strategy involve the use of surrogacy.\(^{[21]}\) According to studies\(^{[8,22,23]}\) the combined use of a gonadotrophin-releasing hormone antagonist protocol with gonadotrophin-releasing hormone agonist triggering and oocyte and embryo freezing has been considerably promising in preventing OHSS, while other studies highlight the ongoing risk of severe OHSS even after these regimen\(^{[5,24,25]}\). OHSS management of moderate...
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OHSS have been reported with high dose cabergoline[26] and continuous vaginal and bilateral thoracic fluid drainage.[27,28] A rare description of octreotide administration as an effective treatment modality of OHSS caused by gonadotropin-secreting pituitary adenomas has been reported.[29] Other complications of OHSS and associated disease conditions have also been reported such as ischaemic stroke due to right middle cerebral artery (MCA) occlusion,[30] but genetic predisposition for spontaneous OHSS[31] and gene variations in the FSH receptor (FSHR) gene have been identified for the very rare cases of spontaneous OHSS,[32] as well as hCG-FSH-receptor interaction additionally are involved in the pathogenesis of OHSS[33]

Contrary to the strong correlation of OHSS with ovulation induction, severe OHSS was reported in spontaneous ovulatory cycles[34–36] and even after delivery usually in the case of multiple gestations, hypothyroidism or polycystic ovary syndrome.[38] OHSS have severally been associated with thromboembolic events[39–45] hence the study on the hereditary and inherited thrombophilia markers.[1] OHSS as an uncommon cause of dyspnoea has been reported and it was indicated that its prevalence is likely to increase.[7] OHSS have been studied to gonadotroph adenoma in a premenopausal woman,[46] and associated with pleural effusion,[47] ischaemic stroke,[48] tubercular ascites[49] and complicated by Stenotrophomonas maltophilia peritonitis.[4]

**CONCLUSION**

The result of extensive review of literature revealed that schistosoma haematobium with OHSS has not been reported and perhaps due to the fact that it is not commonly associated with OHSS; although it is prevalent in Nigeria. Our case report presents an instructive guide to clinicians to always look beyond commonly known correlates such as ureteral injuries or thromboembolic events in patients with OHSS undergoing IVF treatment. This report recommends that in addition to including bladder and ureteric injuries in the differential diagnoses of a patient presenting with abdominal pain following oocyte retrieval, other infectious disease conditions should be investigated.

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**Conflicts of interest**

There is no conflict of interests, be it financial or in any other form.

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