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**Detection of *Borrelia crocidurae* in a vaginal swab after miscarriage, rural Senegal,
Western Africa**

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24 **ABSTRACT**

25 Tick-borne relapsing fever (TBRF) borrelias are one of the main causes of fever in rural
26 Africa and can cause miscarriages. Here, we detected, for the first time to the best of our
27 knowledge, *Borrelia crocidurae* in a self-vaginal sampling as a probable cause of spontaneous
28 miscarriage.

Overdiagnosis of malaria in endemic areas overshadows the presence of other pathogens, such as bacteria that induce fever (Gwer et al., 2007). In Senegal, several studies have already reported the presence of DNA from pathogenic bacteria in the blood of patients with non-malarial fever, including tick-borne relapsing fever (TBRF) borrelia (Mediannikov et al., 2014; Parola et al. 2011; Talagrand-Reboulet al., 2018). TBRF borrelias are risk factors for pregnant women and can cause miscarriages (Giakomelou et al., 2016). *Borrelia* are known to readily penetrate different biological barriers. This is explained by their helical shape and their movement ability and is facilitated by the use of the host protease. In recent years, reliable and effective vaginal self-sampling has been used in the diagnosis of several infections, including HPV and bacteria causing sexually transmitted infections (STI) (Lagier et al., 2017). First, we carried out a project to assess the feasibility of taking vaginal samples in rural areas of Senegal associated with the detection of the carriage of some bacteria or Human papillomavirus, as previously reported (Fall et al., 2019). Our study on miscarriages, which began in March 2016, consists of self-sampling women who have had a miscarriage or other pregnancy problems and determining whether pathogens are responsible for abortions or other pregnancy problems in rural areas of Senegal. To the best of our knowledge, we report here the first detection of *Borrelia crocidurae* in self vaginal sampling in such clinical involvement.

The study was performed in health posts in Dielmo, Ndiop and Niakhar (Diohine, Toucar, Ngayohéme) in Senegal, West Africa (Fall et al., 2019). Women who had miscarriage performed a vaginal self-sampling (Transwab M40 COMPLIANT for bacterial detection). An informed consent was obtained from patients. The ethical authorization for our study was granted by the national ethics committee of Senegal (n°83/MSAS/DPRS/CNFRS). The microorganisms, including those associated with STI and those known to cause abortion, were tested by qPCR and will be the subject of a study published separately. When a sample was

positive for one gene, a second qPCR targeting another gene was performed (Table 1). To check the quality DNA extracts, we tested the human albumin gene as previously described (Fall et al., 2019).

From March 2016 to July 2017 we tested 132 vaginal samples from controls (women living in the same geographic areas and with no history of complicated pregnancy) and 26 vaginal samples from patients. All samples are of great quality (100% positive for human albumin). Using qPCR, we obtained 3 vaginal samples positive for *Borrelia* sp. 16S in patients and none in controls. However, only 1 was confirmed by a qPCR targeting the ITS4 (intergenic spacer) locus. A standard PCR targeting the ITS locus confirmed our diagnosis (Table 1). The sequencing of the ITS locus amplicons (539 base pairs, Genbank accession number: LT984797) exhibited a 100% sequence similarity with *B. crocidurae* (KF176340.1) isolated from *Ornithodoros sonrai*, the vector of borreliosis, collected in the same geographic areas. This sample was collected from a woman who underwent an abortion after 12 weeks of pregnancy. The difference between patients (1/26) and controls (0/132) was significant for *B. crocidurae*. The patient lives in Niakhar area and had a history of 3 spontaneous abortions. The 25 patients who tested negative for *B. crocidurae* had had an abortion from 6 to 24 weeks of pregnancy (mean of 20 weeks). The patient with a positive sample for *Borrelia* lives in an environment with horse, calf, goat, donkey and sheep and has seen many rats in her house but never ticks. Her house was built in bricks and the soil was non-cemented dirt. Floor and walls included some crevices (Figure 1 A and B). The 25 patients who had miscarriage but with a negative sample for *Borrelia* lives in same geographical area and no difference regarding the repartition of animals was observed.

Our study suggests that vaginal self-sampling could be a valuable technique to detect *B. crocidurae*. The use of a consequent number of controls living in the same geographical area and the use of stringent protocols confirm the accuracy of our results. The fact that women

were taking samples from the brick and cement dispensary and not at homes, and the fact that all controls were negative, excluded an environmental contamination of the sample.

Tick-borne relapsing fever (TBRF) is transmitted to humans through the bites of soft ticks of the genus *Ornithodoros*. Wild rodents and insectivores are common reservoir hosts. TBRF is responsible for recurring fever associated with spirochetemia and constitutes the main cause of non-malarial fever in Senegal (Talagrand-Reboulet al., 2018). Previous studies performed in Rwanda and in Tanzania demonstrated a 30% risk for pregnancy loss and a perinatal mortality rate of 15% in case of tick-borne relapsing fever (Talagrand-Reboulet al., 2018). In addition of *Borrelia crocidurae* infections, our study suggests that vaginal self-sampling is a method adapted to the detection of infectious causes of spontaneous miscarriage in low-income countries (Lagier et al., 2017). Certainty of a link between the vaginal detection of *Borrelia crocidurae* and the causality of abortion will require further more in-depth studies. Nevertheless, this technique of sampling could be coupled with Point-of-Care laboratories, which have previously demonstrated their efficiency in exploring the non-malarial causes of fever (Drancourt et al., 2016) and could be used to elucidate the infectious causes of miscarriage in low-income countries.

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CONTRIBUTION

Study design: JCL, DR, CS; Data collection: NSF, ND, JCL; Data analysis: NSF, OM, FF, PP, JCL, CS, DR; Writing: NSF, PP, DR, JCL

CONFLICT OF INTEREST STATEMENT

None

ETHICAL APPROVAL:

The ethical authorization for our study was granted by the national ethics committee of Senegal (n°83/MSAS/DPRS/CNFRS).

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156 **Figure 1:**

157 **A:** Home of the women suffering of miscarriage near Niakhar, Senegal, West Africa with
158 detection of *Borrelia crocidurae* in her self-vaginal swab

159 **B:** Crevices observed in the house

160

161 Table 1: Molecular biology tools used for the identification of *Borrelia crocidurae*

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Gene	Targeted sequence
<i>Borrelia</i> sp. 16S	Bor_16S_3 F : AGCCTTTAAAGCTTCGCTTGTAG, Bor_16S_3R : GCCTCCCGTAGGAGTCTGG, Bor_16S_3P : 6FAM-CCGGCCTGAGAGGGTGAACGG
qPCR targeting the ITS4	Bor_ITS4_F: GGCTTCGGGTCTACCACATCTA, Bor_ITS4_R : CCGGGAGGGGAGTGAAATAG, Bor_ITS4_P : 6FAM- TGCAAAAGGCACGCCATCACC
Standard PCR targeting the ITS locus	ITS F : AGGGGGGTGAAGTCGTAACAAG ITS R : GTCTGATAAACCTGAGGTCGGA

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